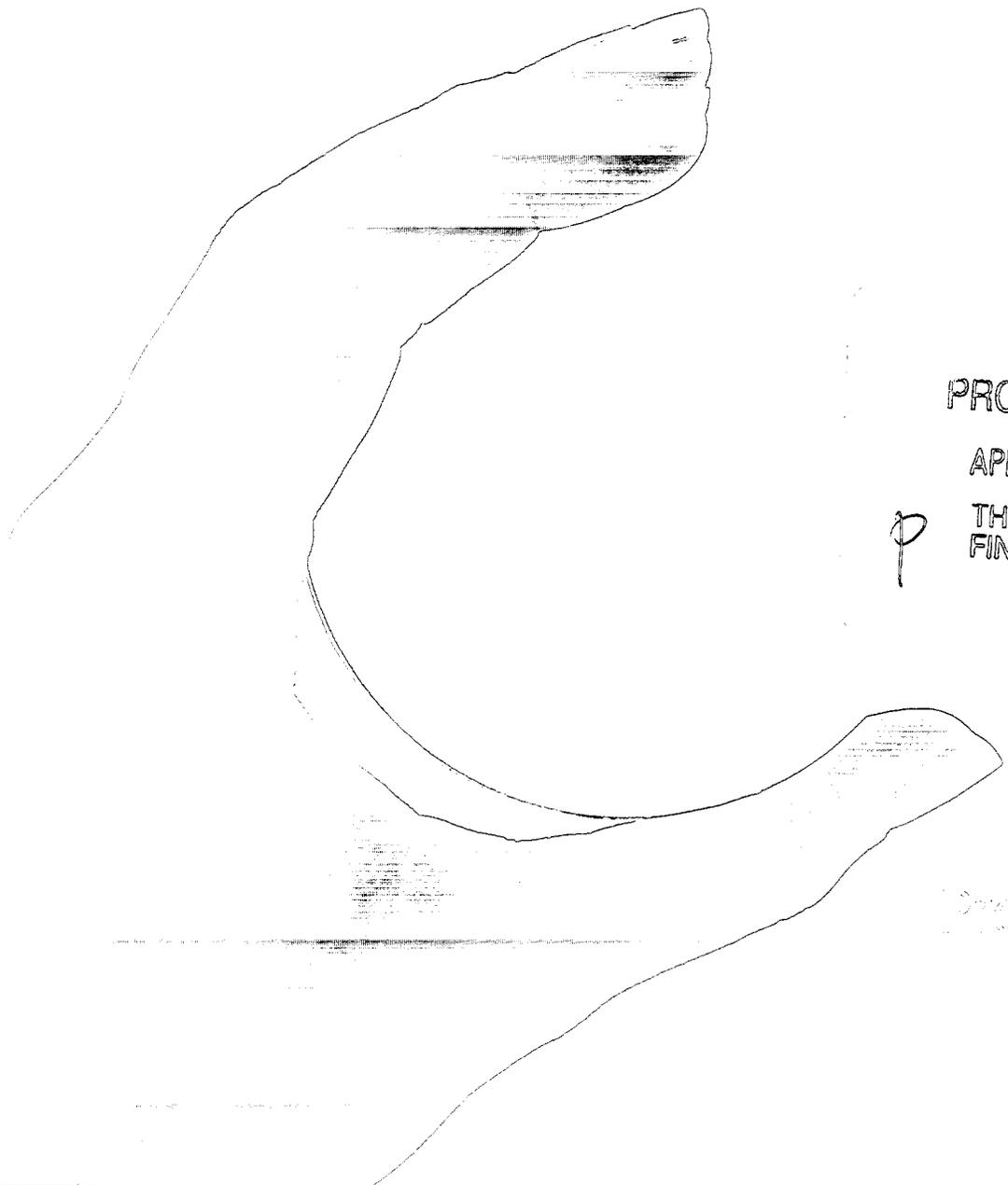


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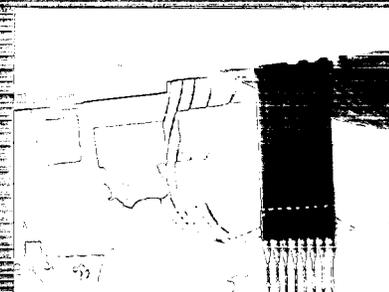
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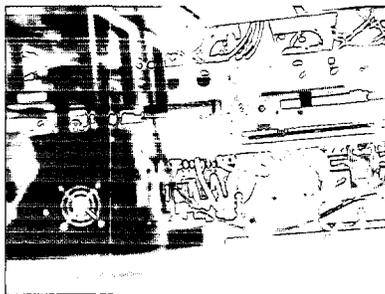


About Vertex

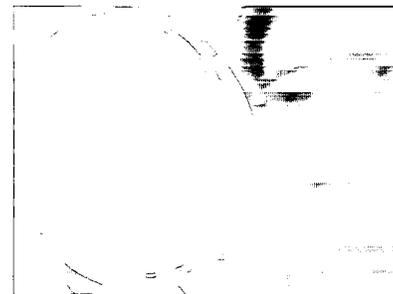
Vertex Pharmaceuticals Incorporated is a global biotechnology company. Vertex seeks to discover, develop, and commercialize major pharmaceutical products both independently and with partners. Chemogenomics, Vertex's proprietary, systematic, genomics-based platform, is designed to accelerate the discovery of new drugs and to expand intellectual property coverage of drug candidate compounds and classes of related compounds. This approach, which targets gene families, has formed the basis for several commercial collaborations that retain rights to downstream revenue for Vertex. Vertex's first approved product is Agenerase[®] (amprenavir), an HIV protease inhibitor, which Vertex co-promotes with GlaxoSmithKline. Vertex has more than 12 drug candidates in clinical and preclinical development to treat viral diseases, inflammation, cancer, autoimmune diseases, neurological disorders, and genetic disorders.

Table of Contents

Vertex Pipeline Milestones	1
Shareholder Letter	2
Pipeline Foldout	4
Products	7
Business Model	9
People	10
Corporate and Shareholder Information	11



3.



4.

1. Medicinal Chemistry, Cambridge, MA
2. High Throughput Assay Development, Madison, WI
3. Discovery Technologies, San Diego, CA
4. Protein Production, Madison, WI

Vertex product developments

2001 Highlights

- ✓ Enrollment completed in 2 of 3 Phase III clinical trials to support product registration for Vertex and GlaxoSmithKline's next-generation HIV protease inhibitor, VX-175 (908)
- ✓ Major Phase II study initiated by partner Aventis of pralnacasan, an oral interleukin-1 beta converting enzyme (ICE) inhibitor, for the treatment of rheumatoid arthritis
- ✓ Advancement of VX-950, first publicly-reported oral drug candidate targeting HCV protease, into preclinical development with Eli Lilly
- ✓ A total of four drug candidates advanced into preclinical development
- ✓ Acquired Aurora Biosciences and PanVera Corporation, increasing the scale of Vertex's drug discovery platform
- ✓ Gene family-based drug discovery initiatives launched in protease and ion channel gene families, in pursuit of multiple therapeutic targets

2002 Goals

- Partner GlaxoSmithKline files new drug application (NDA) for market approval of VX-175 (908)
- Partner Aventis initiates expanded development of pralnacasan
- Initiate clinical development of one or more second-generation p38 MAP kinase inhibitors for inflammation
- Initiate Phase II clinical trial with VX-148, an oral IMPDH inhibitor for psoriasis
- Select four new drug candidates for formal preclinical development, including two or more novel kinase inhibitors
- Advance three drug candidates into clinical development (first-in-man studies)
- Sign new corporate alliances

To Our Shareholders, Employees and Corporate Partners

Vertex's accomplishments in 2001 reflect focused efforts to advance major drug products toward the market and to expand our drug pipeline. Based on progress with a global Phase III clinical program in 2001, we anticipate that our partner GlaxoSmithKline will file for market approval of our next drug, the HIV protease inhibitor VX-175, in the United States and the European Union in 2002. We also achieved important goals with drug candidates at all stages of development, including groundbreaking oral drugs targeting hepatitis C, autoimmune disease, and inflammatory disease. We moved four new drug candidates from our research programs into preclinical development. At the same time, our acquisition of Aurora Biosciences in 2001 has positioned us as a world leader in small molecule drug discovery for a wide array of novel and clinically important drug targets. These accomplishments provide a strong foundation for major product advancements in 2002 and beyond, which we believe will create demonstrable value for shareholders.

Clinical and Commercial Progress

Working independently and with partners, we have built one of the broadest and deepest pipelines in the biotechnology industry. Our discovery engine has generated more than 12 small molecule drug candidates, many of which represent potentially significant medical breakthroughs as "first-in-class" treatments. Our first drug, the HIV protease inhibitor Agenerase[®], is now taken by more than 14,000 patients across 34 countries. Agenerase provides therapeutic benefit and longer life for many patients who do not have other treatment options. Importantly, Agenerase has established a commercial base for the introduction of VX-175 (also known as 908), a next-generation HIV protease inhibitor. More than 1,100 patients are taking part in GlaxoSmithKline's state-of-the-art pivotal trial program, which will be completed this year. We look forward to regulatory filings for market approval of VX-175 in the United States and Europe toward the end of 2002.

We are developing innovative therapies to treat hepatitis C virus (HCV) as well. Approximately 2.7 million people in the U.S. are chronically infected with HCV, a serious disease which can progress to fibrosis, cirrhosis, liver cancer, and death. Our lead drug candidate, merimepodib (VX-497), indirectly targets HCV by blocking the activity of the cellular enzyme IMPDH and robbing HCV of the building blocks it requires to replicate. In 2001, we completed laboratory studies showing that merimepodib may provide added antiviral activity in combination with pegylated interferon and ribavirin, two drugs comprising the current standard of care in HCV treatment. A 12-month triple combination therapy trial is underway to assess the safety, pharmacokinetics and clinical activity of merimepodib,

pegylated interferon and ribavirin in treatment-refractory patients. Should merimepodib meaningfully increase viral clearance in HCV patients, it could emerge as an important HCV treatment option.

We are also pursuing approaches that directly block HCV replication. The advancement of the HCV protease inhibitor, VX-950 (LY570310), into preclinical development in 2001 in collaboration with Eli Lilly is an unprecedented discovery milestone. A drug that directly and potently inhibits HCV protease could be a major weapon in the HCV therapeutic arsenal. We and Eli Lilly are enthusiastic about the clinical and commercial potential for HCV protease inhibitors.

In the area of inflammatory disease, we are pursuing distinct and powerful anti-cytokine approaches by targeting two different enzymes, ICE and p38 MAP kinase. The clinical benefit of cytokine modulation has been proven by injectable agents such as Enbrel[®], Remicade[®], and Kineret[®], which collectively surpassed \$1 billion in sales in 2001. Like these agents, our oral drug candidates seek to control both the acute symptoms and the underlying mechanisms of disease. We believe that the convenience of oral dosing could provide significant clinical and market advantages.

Together with Aventis, we are developing pralnacasan (VX-740), an oral inhibitor of ICE, a human enzyme that regulates activation of the cytokines interleukin-1 beta (IL-1 beta) and interleukin-18 (IL-18). Both IL-1 beta and IL-18 have been implicated in a wide variety of inflammatory processes. In 2001, Aventis began a Phase II study in 250 patients with rheumatoid arthritis, with the goal of evaluating pralnacasan's ability to relieve signs and symptoms as well as modify the course of the disease. As part of a plan to develop pralnacasan in parallel for multiple diseases, we anticipate that Aventis will initiate development of pralnacasan in an additional indication in 2002.

In our p38 MAP kinase program, we are developing therapies with broad potential. The p38 enzyme triggers the production of TNF-alpha, a cytokine implicated in numerous inflammatory disorders, and also drives the production of the cytokines IL-1 and IL-6. In 2001, we experienced a setback with our lead p38 inhibitor, VX-745, based on adverse effect findings in nonclinical studies. At the same time, however, we obtained clinical data demonstrating "proof of principle," which correlated p38 inhibition with a significant clinical anti-inflammatory effect — an industry first. We expect to report this data in the second quarter of 2002. We also expect to initiate Phase I clinical studies in 2002 with at least one of our second-generation compounds, VX-702 and VX-850, reflecting our commitment to remain at the forefront of p38 MAP kinase inhibitor product development.



Increased Productivity in Drug Discovery

We have advanced nine new drug candidates into development over the past two years, demonstrating a pace of productivity that is increasingly driven by our gene family-based discovery approach. Our strategy of targeting entire families, which we call chemogenomics, clusters protein targets according to structural similarity in order to speed drug design. As part of a major collaboration with Novartis, we are targeting protein kinases, a family of 500 enzymes, many of which play key roles in major diseases. Our drug design progress has been strong and we anticipate bringing two or more specific kinase inhibitors into preclinical development in 2002. In total, we expect to advance four or more new drug candidates into preclinical development this year.

World Class Discovery Capabilities

Our acquisition of Aurora Biosciences in 2001 dramatically enhances our product creation capabilities. Aurora's technologies and expertise add a new dimension to our multi-target kinase research program by allowing us to incorporate novel analytical and high throughput technologies into early drug development. Aurora's technology base is also catalyzing a focused expansion of our gene family-based drug discovery efforts into ion channels, a major class of important drug targets. Aurora has developed world-leading capabilities in the sensitive, rapid and information-rich screening of compounds targeting ion channels. In 2002, we are integrating this expertise with Vertex's medicinal chemistry and modeling capabilities, investing more than \$25 million to expand our state-of-the-art ion channel drug discovery program at our San Diego research facility.

An Integrated Business Model

Following the integration of Aurora, we have the ability to pursue new collaborative and product opportunities. We are actively exploring the potential for broad-based partnerships targeting proteases and ion channels. Aurora has created a solid customer base built upon expertise in assay development and high throughput screening, and this adds an important complementary facet to our business model. PanVera Corporation, a Vertex subsidiary based in Madison, WI, continues to rapidly expand product lines of valuable, research-scale proteins and related assay tools, derived independently as well as from Aurora assay research and Vertex drug discovery. We will maintain our focus on our core drug discovery and development capabilities while maximizing the return from the Aurora and PanVera businesses.

Organizational Growth

With more than 1,000 employees at four sites in San Diego, CA, Madison, WI, Oxford, UK, and Cambridge, MA, Vertex is a global company. We have made a focused effort to bring top leadership to this enterprise: over the past year, Ian Smith joined as Vice President and Chief Financial Officer, Kenneth Boger joined as Senior Vice President and General Counsel, Tony Coles joined as Senior Vice President, Commercial Operations — Pharmaceutical Products, and Michael Wokasch was appointed as President of Aurora Biosciences and PanVera Corporation.

Financial Strength

We ended 2001 with cash and investments in excess of \$740 million. Our financial strength is a strategic asset, allowing us to fund new discovery programs, independently develop our own products, and invest in new technologies. For the full 2001 year, we reported a loss of \$45 million, or \$0.60 per share, before merger-related costs and non-recurring charges and gains. Going forward, we are committed to prudent management of our resources as we pursue our product development and commercialization goals.

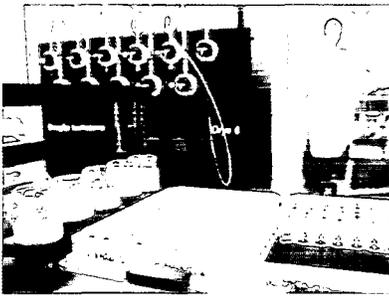
Looking Ahead

Commercializing breakthrough drugs is a complex but highly rewarding endeavor. We manage risk and maximize value creation and commercial return by advancing multiple drugs for major diseases, independently and with partners. We believe that product advances in 2002 will bring us demonstrably closer to our clear corporate goal of sustained revenue growth and profitability. We thank you for your continued support and look forward to sharing news of our progress throughout the year.

Joshua S. Boger, Ph.D.
Chairman and Chief Executive Officer

Vicki L. Sato, Ph.D.
President

March 26, 2002



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1. Medicinal Chemistry, Oxford, UK
2. Clinical Development, Cambridge, MA
3. Pharmaceutical Operations, Cambridge, MA

Development

Phase I

Phase II

Phase III

Market

< In 2001, Vertex and Eli Lilly became the first companies to announce the advancement of an HCV protease inhibitor into preclinical development.

< Rheumatoid arthritis is a lead indication for Vertex's p38 MAP kinase inhibitor program.

< Vertex expects to begin a Phase II clinical trial of VX-148 in psoriasis during the second half of 2002.

< Vertex anticipates expanded development of pralnacasan with partner Aventis in 2002.

< As a once- or twice-daily HIV protease inhibitor, VX-175 represents a potentially important clinical advance.

Product creation, value creation

From a competitive advantage in small molecule drug discovery, Vertex has built a broad pipeline of drug candidates targeting major diseases. Based on their mechanism of action, many of these drug candidates have potential application in more than one clinical indication. Vertex's next drug, the HIV protease inhibitor VX-175, is scheduled to be filed for approval by year-end 2002. Research output is accelerating; Vertex has advanced nine drugs into preclinical development in the past two years, and expects to bring an additional four into preclinical development in 2002.

Tear here for easy reference.

	Drug Candidate <small>Partner Region</small>	Research	Preclinical
Antiviral Medicines	<p>Agenerase® (HIV Infection) <i>GlaxoSmithKline Worldwide</i></p> <p>VX-175 (HIV Infection) <i>GlaxoSmithKline Worldwide</i></p> <p>merimepodib (HCV Infection)</p> <p>VX-950 (HCV Infection) <i>Eli Lilly Worldwide</i></p> <p>VX-799 (Sepsis) <i>Serono (option) Taisho (option)</i></p> <p>VX-385 (HIV Infection) <i>GlaxoSmithKline Worldwide</i></p> <p>DNA Gyrase Inhibitor (Bacterial Infection)</p>		
Anti-inflammatory Medicines	<p>pralnacasan (Rheumatoid Arthritis) <i>Aventis Worldwide</i></p> <p>VX-765 (ICE Inhibitor)</p> <p>VX-702 (p38 Inhibitor) <i>Kissei Pharmaceuticals Far East</i></p> <p>VX-850 (p38 Inhibitor)</p> <p>VX-148 (IMPDH Inhibitor)</p> <p>VX-944 (IMPDH inhibitor)</p>		
Neurophillin Ligands	<p>Neurophillin Ligands <i>Schering AG (option)</i></p>		
Antibiotics	<p>Incel™ (Multidrug Resistance Inhibitor)</p> <p>VX-853 (Multidrug Resistance Inhibitor)</p>		
Anti-cancer Medicines	<p>VX-563 (Histone Deacetylase Inhibitor)</p>		
Other	<p>Kinase Inhibitors (Multiple Indications) <i>Novartis Worldwide</i></p>		

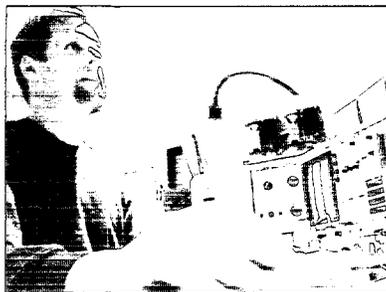
As part of a major kinase research collaboration with  Novartis, Vertex anticipates advancing two kinase inhibitors into preclinical development in 2002.



Creating major **new drug** categories



1. Discovery Biology, San Diego, CA
2. X-ray Crystallography, Oxford, UK
3. Genomic Pharmacology, Cambridge, MA
4. Discovery Technologies, San Diego, CA
5. Combinatorial Chemistry, Cambridge, MA



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Breakthrough drugs for serious diseases

Product discovery — the successful design and synthesis of a new drug candidate — marks an important inflection point in the creation of value in the pharmaceutical industry. Vertex has built a distinct competitive advantage in small molecule drug discovery, with a goal of bringing a steady stream of breakthrough products to the marketplace. With one drug on the market and more than 12 drug candidates in development targeting a range of major diseases, we have built significant value while progressing towards this overarching commercial goal.

We have focused on designing and developing drugs with substantial advantages over existing therapies. The next Vertex-discovered drug to be commercialized, VX-175, has the potential to be an important therapeutic option for the treatment of HIV infection. In the clinical management of HIV infection, there is a focus on creating regimens that are easier for patients to take. In pivotal trials now being completed by our partner GlaxoSmithKline (GSK), VX-175 is being investigated in both once- and twice-daily regimens, with a total pill requirement that is less than half that of the current market leader. We and GSK are optimistic about the market opportunity for VX-175.

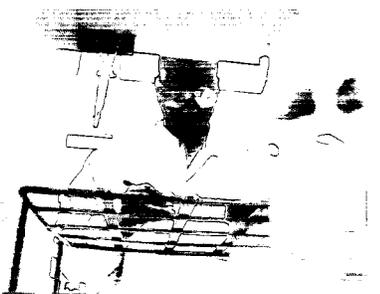
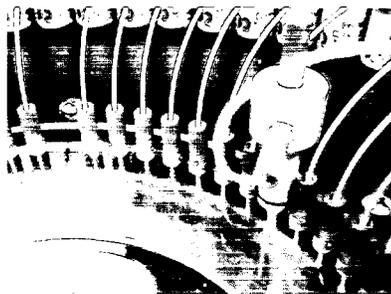
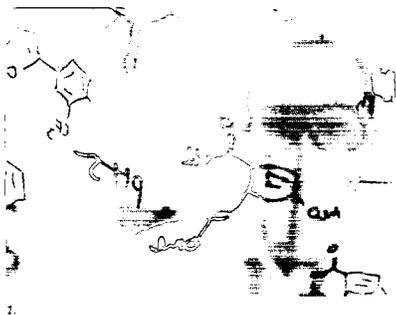
In many cases, we are targeting novel and important molecular mechanisms, creating and advancing drug candidates that, if commercialized, would represent entirely new product categories. One example is pralnacasan (VX-740), an oral inhibitor of interleukin-1 beta converting enzyme (ICE), in Phase II clinical development for the treatment of rheumatoid arthritis as part of a worldwide collaboration with Aventis. Pralnacasan is positioned to be a potent, well-tolerated, first-in-class medicine that targets the reduction of the key inflammatory mediators IL-1 and IL-18 at the core of the inflammatory process.

Pralnacasan is just one of six Vertex-discovered drugs with the potential to fundamentally change medical practice in the area of autoimmune and inflammatory disease. We are independently developing the IMPDH inhibitor VX-148 as an oral drug for the treatment of psoriasis, with the goal of starting Phase II clinical development in 2002. We are also a leader in the development of small molecule p38 MAP kinase inhibitors for the treatment of inflammation, and anticipate initiating Phase I clinical development with at least one novel p38 MAP kinase inhibitor this year.

Vertex's product creation capabilities have consistently distinguished the Company among its biotechnology peers. These capabilities are increasing and expanding. In 2001, we and Eli Lilly advanced a small molecule hepatitis C protease inhibitor, VX-950, into preclinical testing. Drugs such as VX-950 that directly attack hepatitis C viral replication mechanisms could usher in a sea change in the treatment of chronic HCV infection, which afflicts 2.7 million people in the United States alone.

Our pipeline is expanding rapidly, with nine new drug candidates entering preclinical development in the past two years. In 2002, we expect to select four new compounds for preclinical development and initiate clinical studies with three small molecule product candidates. In tandem with this early stage progress, we will continue to drive product development programs forward to the marketplace in 2002. The expansion and advancement of our pipeline is a powerful indicator of our ability to create and build value, positioning Vertex for sustained clinical and commercial success in the years ahead.

Building sustainable value from **innovation**



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1. Medicinal Chemistry, Oxford, UK
2. Molecular Cloning, Cambridge, MA
3. Protein Expression, Madison, WI
4. Biophysical Chemistry, Cambridge, MA
5. Business Development and Marketing, Cambridge, MA



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An industry leader and respected partner

Vertex's business model seeks sustained revenue growth and profitability through development and commercialization of major drugs, both independently and with partners. Our acquisition in 2001 of Aurora Biosciences and its subsidiary, PanVera Corporation, significantly strengthens our ability to realize this goal. The integration of Aurora's technologies and expertise enables us to scale our gene family-based drug discovery approach, enhances our product creation capability, and positions Vertex to build substantial value moving forward.

The integration of Aurora is progressing well; Aurora technologies and expertise are already boosting our drug discovery efforts in the kinase and protease gene families. For example, Aurora's proprietary Biosensor cell panels are providing valuable insights into kinase signaling pathways and helping us select the most appropriate targets for small molecule product development. At our San Diego site, Aurora capabilities are driving a considerable expansion of our drug discovery efforts directed at ion channels, a major class of membrane-bound drug targets. Aurora's technologies will also play an important role as we seek to establish therapeutic proof of principle of our drug candidates in early clinical testing.

Separate and distinct from these focused drug discovery initiatives, Aurora and PanVera are operating as subsidiaries, providing market-leading assay development, screening technologies and reagents to companies in the pharmaceutical industry. Historically, Aurora and PanVera have been partners of choice based on their superior technology and expertise. We continue to see a strong demand for next-generation products and screening capabilities. Moving forward, we will continue to capture the synergies between our businesses, seeking opportunities to broaden our commercial base.

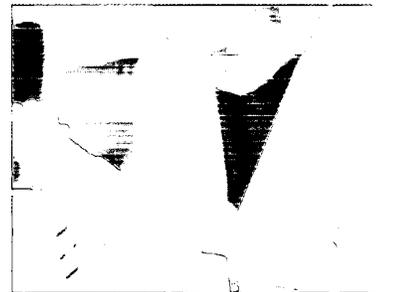
The discovery and development of breakthrough medicines is Vertex's core business. Historically, drug discovery and development alliances with major pharmaceutical companies have enabled us to access development and marketing expertise as well as use our own resources to expand our discovery and development capabilities. Vertex has downstream-focused agreements worth more than \$1.4 billion in pre-commercial payments with major pharmaceutical companies, including Novartis, GlaxoSmithKline, Aventis, and Eli Lilly. These collaborations provide important commercial rights in the form of royalties, profit sharing, co-promotion of products, and/or manufacturing rights to new drugs designed by Vertex.

In the years ahead, collaborative product discovery and development agreements with pharmaceutical partners will continue to be important, as they will allow us to further expand our research base and leverage our core capabilities. We will continue to evaluate collaborative partner opportunities to ensure that we maximize the return of our discovery assets. At the same time, we will also continue to drive forward development of some products independently. This balanced development and commercial strategy is designed to enhance the revenue potential of Vertex's discoveries and in turn provides the potential for significant value creation for shareholders.

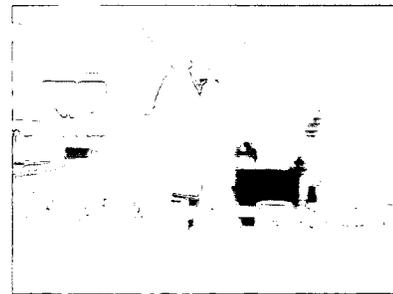
1. *Fluorescence and Ion Channel Modulator Chemistry, San Diego, CA*
2. *Protein Expression, Cambridge, MA*
3. *Medicinal Chemistry, Oxford, UK*
4. *Enzymology, Cambridge, MA*



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A window into Vertex

Our goal is to lead the biotechnology industry in the discovery and product development of first-in-class medicines that offer fundamental improvements to treating serious diseases. Our progress towards that goal reflects the collective efforts of talented employees around the world. We remain fully focused on leveraging our competitive organizational advantages as we seek to scale our product creation ability across the target-rich areas of the genome.

A diverse and creative talent base and a highly integrated corporate culture have long distinguished Vertex. Throughout our history, we have grown our organization thoughtfully and deliberately, recruiting individuals with an insatiable drive to explore and innovate. Today, as then, our mission requires enthusiasm, a sense of urgency, a desire to share knowledge, and the highest degree of integrity. These attributes, when developed to their full potential, inspire great discoveries and ethical, responsible product development.

Vertex is a global business. We have development and commercial partners on three continents, and more than 1,000 employees across four research and corporate sites. Our commercial presence includes 12 clinical liaison offices in the United States and Europe.

Individually, each of our scientific professionals is distinguished by a track record of outstanding achievement. Working together in our collaborative environment, they represent a substantial knowledge base that has set new benchmarks for efficiency and innovation in the biotechnology industry, enabling the creation of breakthrough small molecule drugs.

Vertex has grown organically and by acquisition — we are committed to maintaining our entrepreneurial spirit while cultivating an environment that fosters personal and professional growth. We continue to recruit seasoned managers with superior industry talent, reflecting the increased scale of our business. The extraordinary potential of Vertex's product pipeline is made possible by the accomplishments and dedication of our people. We are determined to sustain and enhance our organizational strength, with the goal of increasing the value of our enterprise for Vertex and its shareholders.

Many thanks to the Vertex employees photographed in this report:

Inside front cover and Page 1

Pan Li (1)
Kevin Loniello, Jason Leduc & Jane Beebe (2)
Laurie Volak (3)
Marie Christenson (4)

Pages 4-5

Graham Cheetham (1)
Steven Knox & Maria Cincotta (2)

Pages 6-7

Rose Isidro (1)
Kieron Brown (2)
Suchitra Chari (3)
Eric Hare (4)

Pages 8-9

David Millan (1)
Ron Smith (3)
Jim Jernee (4)
Leland Webster & Sandra Lauterbach (5)

Pages 10-11

Toby Houchens (1)
Walter Kim (2)
John Studley (3)
William Taylor (4)

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2001

Commission file number 000-19319

Vertex Pharmaceuticals Incorporated

(Exact name of registrant as specified in its charter)

Massachusetts
(State of incorporation)

04-3039129
(I.R.S. Employer
Identification No.)

130 Waverly Street
Cambridge, Massachusetts
(Address of principal executive offices)

02139-4242
(Zip Code)

(617) 444-6100

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(g) of the Act:

Common Stock, \$0.01 par value
(Title of class)

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

As of March 26, 2002 there were outstanding 75,334,652 shares of Common Stock, \$.01 par value per share. The aggregate market value of shares of Common Stock held by non-affiliates of the registrant, based upon the last sales price for such stock on that date as reported by the Nasdaq Stock Market, was approximately \$2,058,900,000.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2002 Annual Meeting of Stockholders to be held on May 17, 2002 are incorporated by reference into Part III.

FORM 10-K INDEX

	<u>Page</u>
PART I	
Item 1. Business	1
Executive Officers and Directors	28
Scientific Advisory Board	30
Risk Factors	31
Item 2. Properties	38
Item 3. Legal Proceedings	38
Item 4. Submission of Matters to a Vote of Security Holders	39
PART II	
Item 5. Market for the Registrant's Common Equity and Related Stockholder Matters	39
Item 6. Selected Consolidated Financial Data	40
Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operation	41
Item 7a. Quantitative and Qualitative Disclosures about Market Risk	52
Item 8. Financial Statements and Supplementary Data	52
Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	52
PART III	
Item 10. Directors and Executive Officers of the Registrant	53
Item 11. Executive Compensation	53
Item 12. Security Ownership of Certain Beneficial Owners and Management	53
Item 13. Certain Relationships and Related Transactions	53
PART IV	
Item 14. Exhibits, Financial Statement Schedules and Reports on Form 8-K.	53

The "Company," "Vertex," "we" and "us," as used in this Annual Report on Form 10-K, refer to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation, and its subsidiaries.

"Vertex," "UHTSS" and "Beacon" are registered trademarks of Vertex, and "Incel," "GeneBLAzer," "GenomeScreen," "Vivid" and "PhosphoryLIGHT" are trademarks of Vertex. "Agenerase" is a registered trademark of GlaxoSmithKline. "Prozei" is a trademark of Kissei Pharmaceutical Co., Ltd. Other brands, names and trademarks contained in this Annual Report are the property of their respective owners.

Forward-Looking Statements

Our disclosure in this Annual Report on Form 10-K contains some forward-looking statements. Forward-looking statements give our current expectations or forecasts of future events. You can identify these statements by the fact that they do not relate strictly to historical or current facts. Such statements may include words such as "anticipate," "estimate," "expect," "project," "intend," "plan," "believe" and other words and terms of similar meaning in connection with any discussion of future operating or financial performance. In particular, these statements include, among other things, statements relating to:

- our business strategy;
- our predicted development and commercial timelines;
- the selection, development and approval of our products;
- the establishment and development of collaborative partnerships;
- our ability to identify new potential products;
- our ability to achieve commercial acceptance of our products;

- our ability to scale up our manufacturing capabilities and facilities;
- the potential for the acquisition of new and complementary technologies, resources and products;
- our projected capital expenditures; and
- our liquidity.

Any or all of our forward-looking statements in this Annual Report may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in our discussion in this Annual Report will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may vary materially. A more detailed reference to our forward-looking statements can be found under "Forward-looking Statements" in Item 7 of this Annual Report.

We provide a cautionary discussion of risks and uncertainties under "Risk Factors" in Item 1 of this Annual Report. These are factors that we think could cause our actual results to differ materially from expected results. Other factors besides those listed there could also adversely affect us.

PART I

ITEM 1. BUSINESS

We are a biotechnology company that seeks to discover, develop and commercialize novel small molecule drugs that address significant markets with major unmet medical needs, including the treatment of viral diseases, cancer, autoimmune and inflammatory diseases, and neurological disorders. Our drug design platform integrates advanced biology, chemistry, biophysics, automation and information technologies to make the drug discovery process more efficient and productive. To date, we have discovered and advanced one product that has reached the market—the HIV protease inhibitor Agenerase® (amprenavir)—and we have more than 12 additional drug candidates in development.

We intend to commercialize some of our products independently and some with collaborators. We have collaborations with Aventis, Eli Lilly, GlaxoSmithKline, Kissei, Novartis, Schering AG (Germany), Serono and Taisho and other companies. These collaborations provide us with financial support and other valuable resources for our research programs, development of our clinical drug candidates, and marketing and sales of our products. We believe that we are positioned to commercialize multiple products in the coming years, which we expect will generate increased milestone payments, product revenues and royalty payments. We have additional research programs underway, and novel Vertex drug candidates targeting bacterial gyrase, specific kinases, caspases and proteases could enter preclinical studies within the next 12 months. These drug candidates may have application in the treatment of bacterial infection, cancer, inflammation, neurological diseases, and HCV infection.

We believe that the emergence of large amounts of information from genomic research represents an unprecedented opportunity for drug discovery directed at novel biological targets. Chemogenomics, our proprietary, systematic, genomics-based platform, is designed to speed drug discovery as well as to expand intellectual property coverage of drug candidate compounds and classes of related compounds. As part of this approach, we are pursuing a strategy of parallel drug design directed at gene families, which are groups of genes with similar sequences that code for structurally similar proteins. Using this strategy, we seek to identify classes of chemical inhibitors (drug-like molecules) that are applicable for clusters of closely related targets that have different biological functions. We believe that chemogenomics will enhance the speed and productivity of drug design efforts directed at novel biological targets, secure for us valuable intellectual property in gene families of interest, and ultimately result in the discovery, development and market introduction of major new drugs.

We are presently applying our expertise in chemogenomics to focus on the protein kinase, caspase, human protease and ion channel gene families, four areas in which we believe we can leverage our drug design expertise to create product candidates that address a variety of sizable therapeutic indications. In May 2000, we entered into a collaboration with Novartis which could provide us up to \$800 million in pre-commercial payments to discover, develop and commercialize up to eight kinase inhibitors for the treatment of a range of diseases, including cancer, cardiovascular diseases, and inflammatory diseases. The financial and technological support provided by Novartis have enabled us to expand both our infrastructure and our chemogenomics efforts in the protein kinase gene family. Technology and expertise acquired through our acquisition of Aurora Biosciences Corporation in July 2001 are leading to a significant expansion of our drug discovery efforts directed at ion channels, a major class of membrane-bound drug targets, and other drug targets. We anticipate establishing new collaborations with major pharmaceutical companies in order to obtain the funding and resources needed to expand these and other discovery efforts.

Aurora, a wholly-owned subsidiary of Vertex, develops and commercializes technologies, products and services to accelerate the discovery of new medicines by the pharmaceutical and biopharmaceutical industries. Our acquisition of Aurora unites Aurora's industry-leading assay development, screening and cell biology capabilities with our integrated drug discovery expertise, creating a comprehensive, scalable platform which we believe will systematically accelerate drug-candidate output in target-rich gene families.

Over the next few years, we expect to continue our research and development efforts and to bring drug candidates through late stage clinical development and into commercialization. We also expect to license and acquire technologies, resources and products that have the potential to strengthen our drug discovery platform, product pipeline and commercial capabilities.

Marketed and Development Stage Products

Our first product, Agenerase, received accelerated approval from the FDA in April 1999 and was launched in May 1999. Agenerase, which was designed by Vertex, is marketed in the United States, Europe and certain other countries by GlaxoSmithKline. We co-promote Agenerase in the United States and in key countries of the European Union (E.U.). Total sales of the drug worldwide for the twelve months ended December 31, 2001 were \$71.9 million, resulting in \$10.8 million in royalty revenue to Vertex.

Agenerase is the first of many Vertex-discovered products that we intend to commercialize, by ourselves and with partners, in the coming years. The accompanying chart describes our product pipeline. One of our drug candidates is presently in Phase III clinical development, four are presently in Phase II clinical development, one is presently in Phase I clinical development, and eight are in preclinical development.

Drug	Clinical Indications	Phase	Company With Marketing Rights (Region)	Estimated U.S. Patient Population (Millions)
INFECTIOUS DISEASE				
VX-175	HIV	III	GlaxoSmithKline (Worldwide except Far East); Vertex co-promote (U.S. and E.U.)	0.9
Merimepodib (VX-497)	Chronic hepatitis C	II	Vertex (Worldwide)	2.7
VX-950	Chronic hepatitis C	Preclin	Eli Lilly (Worldwide); Vertex co-promote (U.S)	2.7
VX-799	Sepsis	Preclin	Serono (Europe, Vertex profit sharing in U.S.)*; Taisho (Japan and Far East)*	0.7
VX-385	HIV	Preclin	GlaxoSmithKline (Worldwide except Far East); Vertex co-promote (U.S. and E.U.)	0.9

<u>Drug</u>	<u>Clinical Indications</u>	<u>Phase</u>	<u>Company With Marketing Rights (Region)</u>	<u>Estimated U.S. Patient Population (Millions)</u>
INFLAMMATION AND AUTOIMMUNE DISEASE				
Prlnacasan (VX-740)	Rheumatoid arthritis (RA); inflammatory diseases	II	Aventis (Worldwide); Vertex co-promote (U.S. and E.U.)	2.1 (RA)
VX-148	Psoriasis; autoimmune diseases	I	Vertex (Worldwide)	NA
VX-944	Autoimmune diseases	Preclin	Vertex (Worldwide)	NA
VX-850	Inflammatory diseases	Preclin	Kissei (Japan)*; Vertex (R.O.W.)	NA
VX-702	Inflammatory diseases	Preclin	Kissei (Japan); Vertex (R.O.W.)	NA
VX-765	Inflammatory diseases	Preclin	Vertex (Worldwide)	NA
CANCER				
Incel™	Multidrug resistant solid tumor cancers	II	Vertex (Worldwide)	0.5 (tumor incidence in target diseases)
VX-853	Multidrug resistant solid tumor cancers	I/II	Vertex (Worldwide)	0.5 (tumor incidence in target diseases)
GENETIC DISORDERS				
VX-563	Multiple indications	Preclin	Vertex (Worldwide)	NA

* Development option

Research Programs

We have several research programs underway at the discovery stage, including multi-target programs that are representative of our gene family-based drug discovery approach, as well as single-target programs. We expect to advance numerous drug candidates into development in the next several years that are based on this ongoing research.

<u>GENE FAMILY/TARGET</u>	<u>CLINICAL INDICATIONS</u>	<u>COMPANY WITH MARKETING RIGHTS (REGION)</u>
Kinases	Cancer; inflammatory diseases; neurodegenerative diseases	Novartis (Worldwide); Vertex co-promote (U.S. and E.U.)
Caspases	Neurological diseases; cardiovascular diseases	Taisho (Japan and Far East); Serono (R.O.W.); Vertex profit sharing (North America)
Proteases	Viral diseases; neurodegenerative diseases	Vertex (Worldwide)*
Ion channels	Pain; cancer; inflammatory diseases; cardiovascular diseases; metabolic diseases	Vertex (Worldwide)
Phosphatases	Pain, cancer; metabolic diseases; inflammatory diseases; cardiovascular diseases	Vertex (Worldwide)
Bacterial DNA gyrase B	Bacterial infections	Vertex (Worldwide)

<u>GENE FAMILY/TARGET</u>	<u>CLINICAL INDICATIONS</u>	<u>COMPANY WITH MARKETING RIGHTS (REGION)</u>
HCV protease (2 nd generation)	Hepatitis C	Eli Lilly (Worldwide); Vertex co-promote (U.S. and E.U.)
HCV helicase	Hepatitis C	Vertex (Worldwide)
Neurophilins (2 nd generation)	Neurodegenerative disorders	Schering AG (E.U.; Vertex profit sharing in U.S.)

* Vertex retains rights in the protease gene family except for certain targets and compounds covered in existing collaborations

Commercial Product and Clinical Development Programs

We have one product on the market and more than 12 additional drug candidates in clinical and preclinical development to treat viral diseases, inflammation, cancer, autoimmune diseases, neurological disorders, and genetic disorders.

Infectious Disease Programs

HIV/AIDS Program

Agenerase

Our first marketed product is Agenerase (amprenavir), an orally deliverable drug for the treatment of HIV infection and AIDS. We created and developed Agenerase in collaboration with GlaxoSmithKline, using our expertise in structure-based drug design, to address unmet needs in the treatment of HIV. Agenerase received regulatory approval in the U.S. in April 1999, and it is now marketed in more than 30 countries worldwide. GlaxoSmithKline is marketing Agenerase worldwide except for the Far East. We co-promote Agenerase in the U.S. and Europe. In Japan, we collaborated with Kissei Pharmaceutical Co., Ltd., in the development of amprenavir, which is sold by Kissei under the trade name Prozei™. We receive royalties on sales of amprenavir by GlaxoSmithKline and Kissei. We also supply amprenavir bulk drug substance to Kissei. We believe that more than 14,000 patients worldwide take Agenerase as part of combination therapy for the treatment of HIV. Agenerase's share of the HIV protease inhibitor prescriptions in the U.S. was approximately 6.8% as of December 31, 2001.

To support the use of Agenerase in the marketplace, GlaxoSmithKline has undertaken a broad Phase IV clinical program aimed at evaluating the drug's use as part of different drug combinations in a variety of patient populations. In collaboration with GlaxoSmithKline, we have initiated several of our own post-marketing clinical studies.

Kissei received approval for amprenavir under a special fast-track initiative by the Ministry of Health and Welfare in Japan in September 1999. Amprenavir's market launch as Prozei followed shortly thereafter.

We believe that Agenerase is distinguished from other protease inhibitors by its:

- longer half-life, which allows for convenient twice-daily dosing and provides high levels of the drug in the bloodstream;
- ability to be dosed effectively with or without food, providing convenience for patients; and
- lower levels of cross-resistance to other protease inhibitors.

Preliminary data indicate that Agenerase is less associated with high cholesterol and triglyceride levels, and less associated with syndromes of fat redistribution than have been reported for other anti-HIV drugs. Studies are ongoing to confirm this preliminary data. Combination studies of Agenerase and the protease inhibitor ritonavir presented at major medical conferences, including the

8th Conference on Retroviruses and Opportunistic Infections in Chicago in February 2001, suggest that ritonavir significantly boosts levels of Agenerase in the bloodstream in both once-daily and twice-daily dosing regimens. Co-administration with ritonavir has become progressively more frequent in clinical practice as a strategy for achieving maximum antiviral activity, reducing the likelihood of treatment failure (viral breakthrough), and lowering the overall pill count for patients. As of December 2001, more than 60% of Agenerase used in the United States was in combination with ritonavir. In February 2002, Agenerase became the first HIV protease inhibitor indicated as part of a once-daily dosing regimen, based on research results in combination with the protease inhibitor ritonavir.

VX-175

We are developing a second HIV protease inhibitor, VX-175 (also known as GW433908 or 908) as part of the GlaxoSmithKline collaboration. A Phase III clinical program has been initiated by our partner, GlaxoSmithKline. This pivotal program includes trials in both treatment-naïve and treatment-experienced patients. The first study compares VX-175 to nelfinavir in treatment-naïve patients. The second study compares VX-175 in combination with ritonavir, administered once-daily, to nelfinavir in treatment-naïve patients. The third study evaluates both once-daily and twice-daily dosing of VX-175 in combination with ritonavir, compared to lopinavir/ritonavir, in treatment-experienced patients. In all of these studies, patients receive reverse transcriptase inhibitors as part of the combination regimen. More than 1,100 patients have been enrolled in these trials, which are designed to provide a robust data package for anticipated regulatory filings in 2002 for market approval in the U.S. and E.U. VX-175 is a prodrug of amprenavir designed to provide more compact dosing for patients. A prodrug is an inactive compound that is changed metabolically by the body to become active against disease. VX-175 was synthesized at Vertex and then selected for development by GlaxoSmithKline. In view of the large number of pills that HIV infected patients typically require daily as part of combination drug regimens, the prodrug's dosing benefit could provide a material increase in physician acceptance of and patient compliance with this product as compared to currently marketed protease inhibitors.

A Phase II clinical study of VX-175 showed that VX-175 possesses potent antiviral activity and a strong pharmacokinetic and safety profile. Preclinical studies and Phase I studies found that administration of VX-175 delivered amprenavir, the active ingredient of Agenerase, and also showed dose-proportionality. The FDA has given VX-175 fast track designation. Fast track designation is granted to products that may provide significant improvement in the safety or effectiveness of the treatment for a serious or life-threatening disease. GlaxoSmithKline is developing VX-175 and has marketing rights in the United States, Europe and certain countries of the Far East. Vertex currently holds the option to develop and commercialize VX-175 in Japan. Vertex has an option to co-promote the prodrug in the United States and the E.U., and we will receive royalties on any sales of VX-175 by GlaxoSmithKline. We also retain rights to supply bulk drug substance to GlaxoSmithKline.

VX-385

In 2001, GlaxoSmithKline advanced another novel, orally available HIV protease inhibitor, VX-385 (GW640385), into preclinical development. VX-385 is the third drug candidate that GlaxoSmithKline and Vertex have advanced into development as part of an ongoing collaboration to develop and commercialize HIV protease inhibitors. VX-385 is chemically distinct from Agenerase, VX-175, and other currently marketed protease inhibitors.

Background: HIV/AIDS

Infection with the HIV virus leads to AIDS, a severe, life-threatening impairment of the immune system. The World Health Organization (WHO) estimates that approximately 36.1 million individuals worldwide, including approximately 920,000 patients in North America, are infected with HIV.

Protease inhibitors (PIs) are used as part of combination regimens for the treatment of HIV. PIs block the cleavage of HIV polyproteins into active proteins, and result in the production of

non-infectious viral particles. Currently, more than 198,000 of the HIV patients receiving drug treatment in the U.S. take at least one PI. The market for HIV PIs is highly competitive, with seven different PIs vying for a share of the market. Worldwide sales of HIV PIs were an estimated \$1.75 billion in 2000, and U.S. sales alone were an estimated \$1 billion in 2001.

There are now three classes of antiviral drugs approved for the treatment of HIV infection and AIDS: nucleoside reverse transcriptase inhibitors (NRTIs), such as AZT and 3TC; non-nucleoside reverse transcriptase inhibitors (NNRTIs), such as efavirenz; and PIs, including Agenerase.

Hepatitis C Virus (HCV) Infection

Vertex is developing two drug candidates that target hepatitis C viral infection by different mechanisms. The most advanced compound is merimepodib (VX-497), currently in Phase II development. Merimepodib targets hepatitis C indirectly through the inhibition of inosine 5'-monophosphate dehydrogenase. The second compound, VX-950, is in preclinical development. It targets the hepatitis C virus directly, by inhibiting the hepatitis C protease.

Identified in 1989, hepatitis C (HCV) causes chronic inflammation in the liver. In a majority of patients, HCV establishes a chronic infection that can persist for decades and eventually lead to cirrhosis, liver failure and liver cancer. HCV infection represents a significant medical problem worldwide for which there is inadequate or no therapy for a majority of patients. Sources at the Centers for Disease Control and Prevention (CDC) have estimated that approximately 2.7 million Americans, or more than 1% of the population, are chronically infected with HCV, and the WHO estimates that there are as many as 185 million chronic carriers of the virus worldwide. Currently, there is no vaccine available to prevent hepatitis C infection. The current standard treatment of hepatitis C is a combination of pegylated interferon-alpha and ribavirin. At present, however, approximately 50% of patients still fail to show long-term sustained response to pegylated interferon-alpha/ribavirin combination therapy. As a result, new safe and effective treatment options for HCV infection are needed.

IMPDH Program

Vertex is developing novel, orally administered inhibitors of the enzyme inosine 5'-monophosphate dehydrogenase (IMPDH), targeting the treatment of both viral and autoimmune diseases. We retain all commercial rights to merimepodib and second generation compounds resulting from our IMPDH research and development program.

Our lead compound, merimepodib, has demonstrated potent biological activity and oral bioavailability in preclinical and early clinical studies. Data from a Phase I trial in healthy volunteers, completed in 1998, show that merimepodib is well-tolerated in single escalating doses and achieves blood levels well above those necessary to achieve potent inhibition of IMPDH *in vitro*. In November 1999, we announced preliminary data from a Phase II clinical trial of merimepodib indicating that merimepodib, when given as monotherapy to HCV patients who were unresponsive to prior treatment with interferon-alpha, was well tolerated and appeared to reduce levels of serum alanine aminotransferase, a marker of liver inflammation, in HCV patients treated for 28 days.

We conducted a Phase II study of merimepodib combined with interferon-alpha in treatment-naïve patients with HCV infection in order to assess the safety, tolerability and clinical activity of the combination of merimepodib and interferon. The viral load data from this study showed a trend toward enhanced antiviral activity in patients given one of two doses of merimepodib combined with interferon as compared to patients receiving interferon alone. This is consistent with an additive antiviral effect mediated by merimepodib, when given in combination with interferon-alpha. Recent *in vitro* data demonstrates that merimepodib also has an additive antiviral effect in combination with pegylated interferon and ribavirin. We have initiated a 12-month triple combination Phase II study with merimepodib, pegylated interferon, and ribavirin with the goal of evaluating safety, pharmacokinetics, and clinical activity, including an assessment of whether patients show an enhanced additive antiviral

effect as a result of the triple combination. The study is designed to allow patients to exit the study or continue treatment after six months.

We have two additional IMPDH inhibitors, VX-148 and VX-944, in development or preclinical development, targeting antiviral and autoimmune indications. VX-148 and VX-944 are chemically distinct from merimepodib. We began Phase I clinical development of VX-148 in December 2000. Three Phase I studies have been completed. We anticipate moving VX-148 into a Phase II clinical study in an autoimmune indication during the second half of 2002. In addition, we plan to begin Phase I clinical studies of VX-944 this year. More information on VX-148 and VX-944 is available in the section titled Autoimmune Diseases.

Background: IMPDH and HCV

Cells require adequate nucleotide levels to sustain RNA and DNA synthesis. Nucleotides can be made available for nucleic acid synthesis via two distinct pathways, the "salvage pathway" and "*de novo* synthesis." Using the salvage pathway, cells recycle nucleosides derived from breakdown of nucleic acids, whereas with *de novo* synthesis the purine or pyrimidine ring systems of the nucleotides are assembled in a stepwise manner. The enzyme inosine 5'-monophosphate dehydrogenase (IMPDH) catalyzes an essential step in the *de novo* biosynthesis of guanine nucleotides, namely the conversion of inosine 5'-monophosphate (IMP) to xanthosine 5'-monophosphate (XMP).

Different cell types rely on these two pathways of nucleotide biosynthesis to varying degrees. Cells that proliferate relatively rapidly, such as lymphocytes and virus-infected cells, often rely more on the *de novo* pathway because they require more nucleotides than can be provided by the salvage pathway. This observation makes enzymes of the *de novo* pathway an attractive target for pharmacological intervention aimed at selectively inhibiting proliferation of such cells.

Hepatitis C protease Program

In December 2001, Vertex and Eli Lilly selected VX-950 (LY570310), a potent, oral HCV protease inhibitor, for preclinical development. We believe that this compound is the first reported drug development candidate of a new class of antiviral drugs being studied to inhibit hepatitis C NS3-4A protease, an enzyme considered essential for HCV viral replication. We believe that therapeutics such as VX-950 which directly target viral replication may significantly increase the number of patients that achieve a complete viral response, in which the virus is cleared from the body permanently. VX-950 has shown promising results in cellular assays and preclinical studies. VX-950 has the potential to become a first-in-class therapeutic and could provide an important treatment advance for individuals with chronic HCV infection. Under our agreement, Eli Lilly holds primary responsibility for formulation, preclinical and clinical development, and global marketing. We will receive royalties on product sales and retain the option to supply all of Eli Lilly's commercial drug substance supply needs. We have ongoing drug discovery efforts in the area of HCV protease inhibitors and selection of one or more additional drug candidates in the next 12-18 months is possible.

Sepsis

In 2001, Vertex advanced VX-799, a small molecule caspase inhibitor, into preclinical development targeting the treatment of sepsis. Sepsis is a life-threatening bacterial infection of the bloodstream that overwhelms the body's immune system and most commonly occurs among patients who have underlying conditions such as trauma, surgery, burns, cancer and pneumonia. Caspases play integral roles in both programmed cell death and inflammation, which have been implicated in sepsis. Sepsis may progress to multi-organ failure, shock and death. A potent caspase inhibitor may have the potential to provide a powerful treatment option for sepsis patients. Sepsis affects approximately 700,000 individuals in the U.S. each year and an additional 1.2 million in Europe and Japan. Sepsis results in an estimated 200,000 deaths each year.

Vertex is currently conducting a range of preclinical studies with VX-799, and we anticipate that clinical studies will begin in 2003. Under an agreement signed in 2000, Serono S.A. holds an option to

develop and commercialize VX-799 in Europe and as part of a joint venture with Vertex in the U.S. Taisho holds the option to develop and commercialize VX-799 in Japan and certain Asian markets.

Background: Caspases and Sepsis

Caspases are a family of 11 enzymes that play roles in numerous biological processes, including programmed cell death (apoptosis) and inflammation. More information on caspases is available in the section titled "Caspase Inhibitor Program." VX-799 has produced encouraging results in an apoptosis-dependent model of organ failure and several models of bacterial-induced sepsis. VX-799 may also have the potential to treat other diseases in which increased caspase activity is implicated.

Inflammation and Autoimmune Disease

Inflammatory Disease

Interleukin-1 Beta Converting Enzyme (ICE; caspase-1) Program

We are conducting research and development on inhibitors of interleukin-1 beta converting enzyme (ICE; caspase-1) for the treatment of acute and chronic inflammatory conditions, including rheumatoid arthritis. We are collaborating with Aventis S.A. in the development of the lead ICE inhibitor compound, pralnacasan (VX-740). Aventis is conducting a 250 patient Phase II study in rheumatoid arthritis to evaluate clinical activity using standard measures of response to treatment, including the American College of Rheumatology (ACR) response criteria, which measure improvement in patient- and professionally-reported disease severity and activity. We anticipate that Aventis will begin a Phase II study in an additional indication in 2002. Inhibitors of ICE may have application to a wide range of chronic and acute inflammatory diseases, such as rheumatoid arthritis, osteoarthritis, congestive heart failure, psoriasis and inflammatory bowel disease.

In 2000, Aventis completed a Phase IIa 28-day clinical trial of pralnacasan in patients with rheumatoid arthritis to evaluate the safety and pharmacokinetics of multiple doses of pralnacasan. Results showed dose-dependent suppression of interleukin-1 beta production, an enzyme that plays a role in inflammation and tissue damage. A Phase I clinical trial of the compound, completed by Aventis in 1999, showed that the compound was well-tolerated in humans in a range of single doses. Under our 1999 agreement, Aventis holds an exclusive worldwide license to develop, manufacture and market pralnacasan in any indication, as well as an exclusive option for all other compounds discovered under our previous research collaboration with Aventis. We will receive royalties on any sales of pralnacasan.

Vertex has continued research into second generation ICE inhibitors, as well as other caspase inhibitors. In 2000, we advanced VX-765, an ICE inhibitor representing a chemical class distinct from pralnacasan, into preclinical development. Preclinical data reported in 2001 showed that VX-765 reduces inflammation and cytokine levels in animal dermatitis and arthritis models. We may begin Phase I clinical studies with VX-765 by the end of 2002. We hold worldwide rights to compounds emerging from our second generation ICE inhibitor research program.

Background: ICE Inhibitors for Inflammatory Disease

ICE (caspase-1) is an enzyme that controls the release of active interleukin-1 (IL-1) beta (one of two forms of IL-1) and IL-18 from white blood cells into the bloodstream and within tissues. IL-1 beta and IL-18 are cytokines that mediate a wide range of immune and inflammatory responses in many cell types. Early in the inflammatory process, IL-1 beta is released from white blood cells, initiating a complex cascade of events that results in inflammation and tissue damage. IL-18 is an important factor in the activation of lymphocytes, a type of white blood cell. Elevation of IL-1 beta and IL-18 levels has been correlated to disease state in a number of acute and chronic inflammatory diseases.

Rheumatoid arthritis is the lead indication of the pralnacasan development program. In patients with rheumatoid arthritis, increased activity of IL-1 beta and IL-18 is observed in joint tissues during disease flare-ups, and IL-1 beta and IL-18 are known to activate osteoclasts, a cell type important in bone erosion characteristic of rheumatoid arthritis. In mice in which arthritis is induced by collagen

immunization, treatment with pralnacasan significantly reduces the severity of arthritis compared to vehicle-treatment.

There are more than 6 million patients with rheumatoid arthritis worldwide, including approximately 2.1 million in the United States. The main drugs used to treat rheumatoid arthritis are non-steroidal anti-inflammatory drugs (NSAIDs) such as Motrin (ibuprofen) and Celebrex (celecoxib). These drugs are palliative—they relieve pain and swelling but do not reverse or prevent the progression of the disease. Methotrexate is a disease-modifying drug that is widely used, but its use is associated with side effects that include bone marrow suppression and liver toxicity. Even when tolerated well, over the long term many patients become unresponsive to methotrexate. Newer therapies including Enbrel® (etanercept) and Remicade® (infliximab) provide a strong rationale for a new kind of disease-modifying therapy that involves inhibition of the cytokine tumor necrosis factor (TNF) alpha. In 2001 Kineret® (anakinra) became the first therapy approved for rheumatoid arthritis targeting the cytokine IL-1b. However, these agents are injectable, and can be inconvenient and painful to administer. We believe that an oral cytokine inhibitor such as pralnacasan may have significant commercial advantages.

Vertex and Aventis scientists began collaborating in 1993 to discover and develop orally available inhibitors of ICE. Our design efforts were based on the three-dimensional atomic structure of ICE, which was solved by Vertex researchers in 1994. As the result of an extensive, jointly conducted synthesis and research program, pralnacasan was selected as a development candidate in 1997. Pralnacasan is the first caspase inhibitor to be advanced to Phase II clinical trials.

p38 MAP Kinase Program

The p38 MAP kinase is a human enzyme involved with the onset and progression of inflammation and apoptosis. This enzyme plays a central role in regulating the cytokines TNF-alpha and IL-1 beta. We have extensive clinical experience with p38 MAP kinase inhibitors, which hold the potential to be a powerful and broadly useful new class of oral anti-inflammatory drugs. Vertex and Kissei selected VX-745 as a drug development candidate in 1998. In 2001, we obtained what we believe is the first clinical “proof of principle” data correlating inhibition of p38 MAP kinase with a significant anti-inflammatory effect, although we subsequently suspended development of VX-745 based on adverse neurological effect findings in long-term, high dose studies in one of two species of animals. We have refocused our p38 inhibitor development efforts around two second generation compounds, VX-702 and VX-850, which do not cross the blood brain barrier and which we believe have commercial advantages over VX-745. Phase I studies of one or both drug candidates are scheduled to begin in the first half of 2002. Both VX-850 and VX-702 represent chemical classes that are distinct from VX-745. The objective of our research collaboration with Kissei is to identify and extensively evaluate compounds that target p38 MAP kinase to develop novel, orally active drugs for the treatment of inflammatory diseases, such as rheumatoid arthritis, asthma, Crohn’s disease, certain hematologic disorders, congestive heart failure, and neurological diseases such as stroke.

In a collaboration with Kissei that began in 1997, Vertex is pioneering the discovery and development of novel p38 MAP kinase inhibitors. Under the agreement, Vertex holds development and commercial rights in the United States and Europe for its p38 MAP kinase inhibitors. Kissei holds development and commercial rights in Japan and certain Asian countries for VX-745 and VX-702.

Background: p38 Inhibitors for Inflammatory Disease

The mitogen-activated protein (MAP) kinases are a family of structurally-related human enzymes involved in intracellular signaling pathways that enable cells to respond to their environment. When activated, the p38 MAP kinase triggers production of the cytokines IL-1, TNF-alpha, and IL-6. Excess levels of IL-1 and TNF-alpha are associated with a broad range of acute and chronic inflammatory diseases. We believe that an oral cytokine inhibitor such as VX-702 or VX-850 has significant dosing advantages over other available therapies.

Excess TNF-alpha and IL-1 levels also play an important role in programmed cell death associated with ischemia and stroke, and possibly in neurodegenerative diseases such as Alzheimer’s disease. We

are aware of several other companies that are developing p38 MAP kinase inhibitors. In addition, there are other drugs, in development or approved, that have different mechanisms of action for treating rheumatoid arthritis and other inflammatory diseases.

Autoimmune Diseases

IMPDH program

Vertex is developing novel, orally administered inhibitors of the enzyme inosine 5'-monophosphate dehydrogenase (IMPDH), targeting the treatment of both viral and autoimmune diseases. In 2000, we designated the second-generation IMPDH inhibitors, VX-148 and VX-944, as drug development candidates. VX-148 and VX-944 are chemical compounds structurally distinct from merimepodib. We are completing Phase I development of VX-148, and Phase II studies are planned to begin during the second half of 2002. Preclinical studies of VX-944 are ongoing.

IMPDH is a validated target for immunosuppressive drug development as evidenced by the presence of two marketed drugs that function through the inhibition of this enzyme:

- Mycophenolate mofetil (MMF, or CellCept®), the prodrug ester of mycophenolic acid, has been developed and approved for the prevention of acute rejection in kidney, heart, and liver transplantation when used in combination with steroids and cyclosporin A (CsA).
- Mizoribine (Bredinin®) is approved in Japan for multiple indications, including prevention of rejection after renal transplantation, idiopathic glomerulonephritis, lupus nephritis, and rheumatoid arthritis.

Based on the broad role of IMPDH in the regulation of immune system activity, we believe that VX-148 has the potential to treat a wide variety of autoimmune diseases including such diseases as psoriasis, multiple sclerosis and rheumatoid arthritis.

Neurological Diseases

Background: Neurological Diseases

Neurodegenerative disorders are among the diseases with the fewest available effective treatments. Central nervous system disorders such as Alzheimer's disease, Parkinson's disease and multiple sclerosis affect millions of patients worldwide, and for some of these there are no approved therapies that alter the course of disease progression. Peripheral neuropathies encompass a wide spectrum of clinical syndromes for which treatments of only limited efficacy are available. Diabetic neuropathy is the most common identifiable cause of neuropathy. There are approximately 1.3 million patients with moderate to severe diabetic neuropathy in the United States.

Effective treatment of both central and peripheral neurological disorders has long been hampered by the inability to slow, arrest, or reverse nerve damage or progression. Other companies are developing various neurotrophic factors (proteins) for these indications, but we believe that their clinical utility is likely to be limited because of the difficulty of the delivery of protein drugs to nervous system tissues. Based on our extensive research in the field of immunosuppressive drugs, we have generated a large number of compounds, known as neurophilin ligands or neurophilin compounds, that improve outcomes in various models of neurological diseases. Extensive *in vitro* and *in vivo* studies conducted with a reference compound designed by Vertex support the broad potential of our neurophilin ligands in the treatment of degenerative central nervous system and peripheral nervous system diseases. Our researchers are seeking to determine the mechanism of action of neurophilin ligands.

Research Compounds

We are engaged in a worldwide strategic collaboration with Schering AG (Germany) for research, development and commercialization of neurophilin ligands for the treatment of a variety of neurological disorders. During 1999, we announced that orally administered neurophilin compounds

discovered at Vertex, including compounds that do not interact with FKBP-12, significantly improve outcome in two different preclinical models of Parkinson's disease. We also reported for the first time that compounds that do not interact with FKBP-12 can improve outcomes in animal models of peripheral neuropathies. We continue to characterize the potential of compounds from this program in a variety of neurological disease models. We have used an integrated drug design technique to synthesize a library of orally available small molecule compounds that have the potential to prevent nerve damage or improve recovery following nerve injury. Our research program remains active in this area, with the objective of selecting additional compounds for preclinical development in the future.

Timcodar

Timcodar dimesylate is a novel, orally administered drug candidate that may be useful in the treatment of neurological disorders such as peripheral neuropathies (including diabetic neuropathy), Parkinson's disease, trauma, and amyotrophic lateral sclerosis (ALS). A single-dose Phase I study of four different doses of timcodar in healthy volunteers was completed in 1998, providing support for Phase II clinical development in the indication of diabetic neuropathy. *In vivo* results in animals have shown that timcodar can prevent neural dysfunction in models of neuropathies. Schering AG has an option to co-develop timcodar with us under the collaboration agreement. We are evaluating novel testing approaches that have the potential to elucidate the clinical activity of timcodar in neuropathies. We have completed a Phase IIa 28-day study of more than 70 patients with diabetic neuropathy. The results showed that timcodar is bioavailable and well-tolerated at a range of doses. An evaluation of timcodar following topical administration of capsaicin in 62 healthy volunteers has also been completed. This study was designed to measure timcodar's ability to accelerate innervation following capsaicin-induced denervation of the epidermal layer. A goal was to obtain data showing that timcodar has a positive effect in recovery of human nerve function. The results of the study indicate that timcodar was well tolerated but did not enhance epidermal nerve fiber regeneration significantly relative to placebo. Given these findings, we do not currently plan to conduct further development of timcodar for the treatment of neurodegenerative diseases.

Cancer

MDR Program

We are developing novel compounds to treat and prevent the occurrence of drug resistance associated with the failure of cancer chemotherapy. Incel (also referred to as biricodar dicitrate or VX-710), our lead compound, blocks major multidrug resistance (MDR) mechanisms, including P-glycoprotein, or P-gp, and multidrug resistance associated protein, or MRP. P-gp and MRP are proteins that are overexpressed on the cell surface of many different tumor types that can prevent the effectiveness of chemotherapy by actively pumping out cytotoxic agents from within the cancer cell. Incel is designed to block these molecular pumps, allowing chemotherapy to affect the targeted tumor. Incel, an intravenous compound, is intended to be administered in combination with cancer chemotherapy agents such as doxorubicin, paclitaxel, vincristine, etoposide and mitoxantrone. We have completed Phase II clinical trials of Incel in ovarian, breast, small cell lung and prostate cancers and in soft tissue sarcoma. An exploratory study has also been conducted in liver cancer. In addition, we have conducted a Phase I/II clinical trial of the compound VX-853, an oral MDR inhibitor, in patients with solid tumors. We retain all commercial rights to Incel worldwide. We are actively seeking corporate collaborators for our MDR program to help support Phase III clinical development and commercialization.

The American Cancer Society estimates that during 2001 more than 1.2 million people in the United States were diagnosed with invasive cancer and more than 550,000 people in the U.S. died from such cancers. A significant number of these patients failed to respond or relapsed following chemotherapy because of MDR.

Genetic Disorders

At the end of 2001, Vertex advanced VX-563 into preclinical development. VX-563 is an orally available compound with potential application across a range of genetic diseases. It is being tested *in vitro*, and *in vivo* in animal models, for several disease indications ranging from sickle cell disease to Huntington's disease. A Phase I clinical study could potentially be initiated in either late 2002 or early 2003.

VX-563 is thought to exert its effects pleiotropically, and we are working to better understand its exact mechanism of action in particular disease states. One mechanism that appears to be important is the inhibition of histone deacetylation. Histones are small proteins that bind tightly to DNA and play a crucial role in the packing and folding of DNA into the nucleus. The acetylation state of histones can modulate gene expression, and VX-563 has been shown to affect histone acetylation *in vitro*.

Preclinical studies have demonstrated that VX-563 can selectively stimulate embryonic or fetal globin gene expression in a variety of experimental systems, suggesting that VX-563 may have therapeutic potential for the treatment of sickle cell disease (SCD). Current treatments are ineffective and may require a multi-disciplinary program including antibiotics, pain management, intravenous fluids, blood transfusion, and surgery. Hydroxyurea is the only chronic drug therapy commonly used to treat SCD. Due to safety concerns, hydroxyurea is currently only used in patients with severe disease.

VX-563 has the potential to be a novel, first-in-class treatment for SCD with the potential to treat as many as 70,000 patients who currently have limited treatment options. VX-563 also has potential application to other genetic disorders such as Huntington's disease, cystic fibrosis, and α -1 antitrypsin deficiency.

Vertex Drug Design Platform and Drug Discovery Strategy

We believe that our integrated drug design approach, together with our strategy of parallel drug design in gene families, has significantly enhanced our ability to discover and develop small molecule drugs directed at biologically complex targets, including novel targets identified in genomic research. Our approach has been validated through our collaborations and success in moving drug candidates into clinical trials.

Integrated Drug Design Approach. Our drug design platform integrates advanced biology, biophysics, chemistry, automation and information technologies in a coordinated and simultaneous fashion throughout the discovery process. The goal of this interdisciplinary integration is to increase the speed and certainty of drug discovery and development. Early in the drug design process, we focus on qualities that are critical to the successful development of oral small molecules, including sufficient potency, oral bioavailability, adequate pharmacokinetics and safety. Our consistent achievement of these parameters in discovery efforts directed at biologically complex molecular targets has been a major reason for our high rate of productivity and success in competitive areas of drug discovery.

Gene Family-Based Drug Discovery. Vertex has pioneered a novel approach to drug discovery in which drugs are designed in parallel across gene families. Vertex's proprietary, systematic, gene family-based platform is designed to accelerate the discovery of new drugs and to expand intellectual property coverage of drug candidate compounds and classes of related compounds. This approach represents an intersection of medicinal chemistry with genomics: the organized pursuit of small molecule drugs directed at genomically identified targets. To date, using our integrated approach, we have been able to design multiple, distinct lead classes of compounds for certain protein targets, and to identify many or all of the critical interactions that a compound must have in order to bind to a target or group of targets. In doing so, we have been able to design and file patent applications covering many of the possible drugs for selected protein targets. For example, in our caspase program, we have obtained a pharmacophore patent that we believe describes a large number of the possible ways of inhibiting caspase-1 with drug-like small molecules, and we believe that chemical scaffolds useful for caspase-1 inhibition may also be useful starting points for inhibiting other targets in the caspase gene family. In

our kinase program, we have filed patents on more than 340 different chemical scaffolds that inhibit one or more kinases.

The complete sequence of the human genome, which represents all of the genes that code for proteins in the human body, is now known. The number of human proteins that represent targets for currently marketed drugs is approximately 500. In the next several years, genomic and proteomic research is expected to reveal as many as 5,000 novel protein targets that represent promising points of therapeutic intervention with small molecule drugs. We believe that the traditional approach to drug discovery, which focuses on one target at a time, is not the most efficient way to exploit this expected increase in the number of "druggable" targets.

To maximize productivity for drug discovery directed at novel protein targets, we are pursuing a strategy of parallel drug design in gene families. This approach applies our integrated strategy across groups of structurally similar targets to pursue rapid and simultaneous generation of lead compounds. Our goal is to use this approach to describe and patent many or all of the possible drug candidates for a protein target or a group of targets. Specifically, we are seeking to:

- design multiple lead classes of compounds that are applicable to clusters of structurally similar targets;
- leverage our knowledge of one target's active site to design inhibitor classes for related targets; and
- identify all of the critical interactions a compound must have to bind to a particular target, and use this information as a basis for obtaining patents that describe many or all of the possible drugs for a target or cluster of targets.

We believe that our integrated approach to drug design is unique among small molecule-based biotechnology companies, and has led to significant collaborations and an extensive intellectual property portfolio covering lead classes of compounds directed at gene families of interest.

We also have a single target research program underway for specific infectious diseases, in areas of high commercial potential and significant unmet medical need.

Multi-Target Research Programs

We have four major multi-target research programs underway that utilize our parallel drug design approach in the kinase, caspase, protease, and ion channel gene families. We believe that our integrated approach and our proprietary technologies allow us to rapidly identify appropriate chemical side chains for these scaffolds that will provide specificity for a particular target of interest within a cluster of related protein targets. In the coming years, we expect to initiate discovery efforts in one or more additional gene families.

Kinase Program

We have a broad-based drug discovery effort targeting the human kinase protein family, which consists of approximately 500 kinases. Kinases are enzymes that play a key role in transmitting signals between and within cells. Kinases exert their effect by phosphorylating other proteins, which then become activated and perform a specific function. Kinases are implicated in most major diseases, including cancer, autoimmune and inflammatory disease, cardiovascular disease, metabolic disease, and neurological disease. Thus, kinases can be ideal targets for intervention with small molecule drugs. In the next six to seven years, we envision advancing eight kinase inhibitors into clinical development targeting multiple therapeutic areas.

We have advanced discovery efforts underway targeting several human MAP kinases. MAP kinases form a group of related enzymes that include extracellular-signal regulated kinase (ERK), p38 MAP kinase, and Jun N-terminal kinase (JNK). As a neuronal-specific isoform of JNK, JNK3 is a member of the MAP kinase family and is implicated in the pathogenesis of certain neurological diseases such as epilepsy, stroke and Alzheimer's disease. We have identified several novel classes of JNK3 inhibitors and are advancing lead compounds toward clinical candidate status. We are also engaged in the discovery of inhibitors of the enzyme ERK2, which plays a role in cell proliferation. We believe that ERK2 inhibitors may have a role in the treatment of cancer. Our p38 MAP kinase inhibitors are discussed earlier in the section titled "Autoimmune and Inflammatory Diseases."

In addition, we have made key research advances in our study of glycogen synthase kinase 3- β (GSK3- β), an enzyme involved in the regulation of blood glucose and a potentially important diabetes target. In June 2001, we reported the three-dimensional atomic structure of GSK3- β . Our understanding of the structural biology of this enzyme is potentially useful in driving medicinal and computational chemistry efforts for enzymes across the entire kinase family.

Vertex has advanced drug discovery efforts underway targeting several additional, undisclosed kinase targets, including targets that play a role in the development and progression of cancer, inflammation and cardiovascular disease. As part of our kinase research program, we have designed numerous kinase inhibitors that have demonstrated pharmacodynamic activity in animal models of diabetes, cancer, restenosis, and stroke. We expect to advance two or more novel kinase inhibitors into preclinical development in the next 12 months.

In May 2000 we entered into an agreement with Novartis Pharma AG to collaborate on the discovery, development and commercialization of small molecule drugs directed at targets in the kinase protein family. Certain targets, where we or Novartis already had a substantial program underway prior to May 2000, are excluded from the collaboration. For example, p38 MAP kinase, which is the molecular target for VX-850 and VX-702, our compounds in development for inflammatory diseases, is not included within the scope of the Novartis collaboration. The financial and technological support provided by Novartis is enabling us to further expand both our infrastructure and parallel drug design efforts in the protein kinase gene family.

Caspase Program

Caspases are a subfamily of proteases which play specific roles in apoptosis and inflammation. The human caspase family presently includes 11 structurally related enzymes. We are designing novel small molecule inhibitors of selected caspase enzyme targets to treat a variety of diseases in which inflammation and apoptosis play a role. Our scientists are leveraging the expertise gained through our successful design and optimization of ICE inhibitors. We applied our knowledge of ICE and other caspases to the design of VX-799, a small molecule caspase inhibitor with the potential to treat sepsis, and we anticipate selecting an additional drug candidate for clinical development in the years to come.

All cells have the ability to self-destruct via a tightly-regulated pathway known as apoptosis in response to certain signals. Apoptosis is an essential component of numerous biological processes, including tissue remodeling and immune system regulation. When not properly regulated, apoptosis can have damaging effects and contribute to a variety of diseases. Our discovery effort is focused on the design of small molecules for inhibiting caspase-mediated apoptotic and inflammatory processes, thereby exerting a protective effect on cells in specific tissues. Potential indications include tissue damage related to acute conditions such as stroke and myocardial ischemia, and neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease.

Through gene knockout studies, our scientists have gained important insight into the biological role of different caspases in the activation of apoptosis in specific cells and tissues. Vertex research teams have solved the three-dimensional atomic structures of four caspases, including one caspase from each of the three caspase subfamilies, and more than 50 enzyme/inhibitor complexes. Different caspases share similar structural features, and by using parallel structural approaches combined with new

medicinal and computational chemistry tools, Vertex scientists made rapid progress in the design and synthesis of multiple lead classes of compounds. Our caspase research effort reflects the implementation of our strategy for exploiting emerging genomic information by targeting families of structurally-related proteins for drug discovery.

In September 1999, Vertex signed an expanded agreement with Aventis to collaborate on the development of pralnacasan, an orally active inhibitor of ICE. In November 1999, we began collaborating with Taisho Pharmaceutical Co., Ltd. to discover, develop, and commercialize caspase inhibitors in Japan and certain Far East markets. In December 2000, we entered into a collaboration with Serono S.A. to discover, develop, and market caspase inhibitors in other territories, including North America, where we have agreed to establish a joint venture with Serono.

Protease Program

We have a broad-based drug discovery effort targeting the human protease family. The protease gene family consists of approximately 400 proteases that play a role in many different diseases in several therapeutic areas. As in our kinase program, we are using an approach that leverages structural similarity to create chemical scaffolds applicable to a range of protease targets. We intend to leverage our expertise in proteases to discover and develop additional drug candidates targeting members of the protease family. We are currently establishing a research program in beta-secretase, an aspartic protease implicated in the pathogenesis of Alzheimer's disease, and will target additional proteases in the coming years.

Vertex has broad experience across the protease family and has successfully designed drug candidates targeting aspartyl, cysteine, and serine proteases, representing three of the four protease subfamilies. Our efforts targeting HIV protease (an aspartyl protease) have resulted in one marketed drug, Agenerase, and two additional drugs in clinical development. Vertex, together with Aventis, Serono and Taisho have pioneered research and development efforts to design drugs targeting caspases (which are cysteine proteases). Our lead drug candidate targeting caspase-1, pralnacasan, is now in Phase II clinical development. We also have two additional drug candidates targeting caspases in development. In 2001, Vertex and Eli Lilly advanced VX-950, an inhibitor of HCV protease (a serine protease), into preclinical development. We believe our extensive experience in proteases will allow us to design additional drugs targeting protease enzymes that have high clinical and commercial potential.

Ion Channel Program

Vertex is making a significant investment in the creation of a broad-based ion channel drug discovery effort that incorporates our medicinal chemistry and modeling expertise, augmented by significant technology and expertise obtained through our acquisition of Aurora. The ion channel gene family contains numerous druggable targets that play a role in the pathogenesis of cancer as well as inflammatory, cardiovascular and metabolic diseases. Existing therapies such as amlodipine and nifedipine, which are calcium channel blockers for the treatment of hypertension, provide a strong rationale for developing drugs targeting ion channels. Important targets for a range of therapeutic indications are potentially found across all ion channel subfamilies. For example, lamotrigine and carbamazepine are sodium channel inhibitors for the treatment of epilepsy. Vertex will utilize its expertise in assay development and screening to advance discovery efforts within this family. We also have extensive experience in the development of proprietary and highly sensitive instruments which detect changes in a cell membrane's electrical potential due to ion channel activity. We are developing next generation ion channel screening technology to enable the discovery of ion channel modulators with appropriate drug-like characteristics.

Additional Gene Families

Vertex plans to utilize its proprietary gene family-based platform and experience in structure based drug design to pursue targets in additional, medically important gene families. We have exploratory efforts underway in phosphatases, G protein coupled receptors (GPCRs), and nuclear receptors.

Single Target Research Program

Bacterial Gyrase

We are engaged in the discovery of novel antibiotics that target DNA gyrase B, an essential enzyme found in many bacteria. DNA gyrase is utilized during the bacterial replication process. DNA gyrase inhibitors already on the market have proven to be potent, broad-spectrum antibiotics and are used to treat a variety of common gram-positive and gram-negative infections in various treatment settings. Existing gyrase inhibitors, which work by interacting with the gyrase A subunit, achieved sales of more than \$2.85 billion in 2000. In contrast, we are targeting the gyrase B subunit, and specifically the ATP-binding site that is highly conserved across multiple species of bacteria. We are currently optimizing lead classes of inhibitors and plan to select a drug development candidate in 2002.

Key Components of Our Technology Platform

We have created an integrated technology platform which employs a variety of technologies, and which uses information from many different scientific disciplines early and continuously throughout the drug discovery process. We believe that our integrated approach, as demonstrated by our track record in drug design directed at biologically complex targets, provides for faster and more productive drug discovery compared to historical averages for the pharmaceutical industry. Selected technologies include:

Genomics and Bioinformatics. We have an agreement with Incyte Pharmaceuticals for access to its Lifeseq Gold database, a comprehensive portfolio of genomic information. We anticipate accessing or acquiring additional technology, as well as information from both public and private databases, to further our parallel drug design strategy.

Functional Genomics. We use a number of functional genomics techniques, such as gene knock-out mice, to help guide target selection and test the potential of chemical compounds in disease models. Site-directed mutagenesis is used to identify critical residues for drug interaction in the active site of a molecular target. Our patented GenomeScreen technology allows us to identify and validate targets by scanning the genome of living human cells and identifying those genes activated or repressed in various disease states. We have used GenomeScreen to assist us in mapping gene activation and cell signaling pathways and in characterizing poorly understood cellular processes.

Biophysics. One of our core strengths is the generation of atomic structural information on molecular targets using X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy to guide design and optimization of lead classes of drugs. Our scientists have also pioneered innovative NMR techniques, including a proprietary technology called NMR SHAPES, which can screen molecular subunits for weak affinity to a molecular target. This initial screening can quickly identify lead classes of molecules for further evaluation.

Computer-based Modeling. We apply advanced, proprietary computational modeling tools to guide early evaluation of compounds. During initial virtual compound screening (*"in silico"*), we can evaluate up to 10^{14} compounds in one day to select fewer than 100 or as many as 1,000 compounds or more for synthesis and traditional screening, and repeat the cycle thereafter based on initial results. By using proprietary algorithms to sort and filter compounds for specific properties, our scientists can efficiently focus on compounds that are more likely to be useful leads.

Medicinal and combinatorial chemistry. Medicinal chemistry expertise is a key part of our drug discovery process. Medicinal chemists visually evaluate each compound that emerges through *in silico*

screening processes and provide insight into the creation of focused libraries for screening. We use combinatorial chemistry to design diverse libraries based on promising early leads.

Pharmacology. We employ a number of approaches designed to provide predictive information on the bioavailability and pharmacokinetic profile of potential compounds at the earliest stages of the drug discovery process. These approaches, which include *in vitro* metabolism and toxicological studies and *in vivo* assessment of leads in predictive animal models, provide greater certainty that a compound will have the desired properties of an oral drug.

Assay Technologies. Our 2001 acquisition of Aurora has provided us with premier capabilities in assay development and screening to rapidly generate large numbers of high quality lead compounds and drug candidates across all major gene families. We can now conduct 200 assays per year, a level of screening capability on par with that of major pharmaceutical companies. We are leveraging our abilities in assay development, screening, proprietary reagents, proteomics, and ADME/toxicology to accelerate drug discovery. Our assay technology platform allows us to identify medically important targets and small, drug-like molecules early in the discovery process.

Assay Development. Our patented cell-based assay technologies include GenomeScreen and GeneBLAzer. GeneBLAzer, which enables fluorescence-activated cell sorting, is readily adapted to a broad range of target classes. In addition, we utilize fluorescence polarization technology to study molecular interactions and have developed a number of proprietary fluorescent proteins and substrates. Drug discovery-related applications of our patented fluorescent proteins include various methods of functional genomics, high throughput screening assays, and gene profiling to assess the potential toxicity of compounds.

High Throughput Screening. Our patented ultra high throughput screening (UHTSS) platform is designed to screen over 100,000 compounds per day. The UHTSS Platform combines compound management, plate replication, assay preparation, hit (potential lead) identification, selection and re-tests of the hits, fluorescence detection and data analysis into one fully-integrated and automated system. The ultra high throughput capability is achieved through the use of our NanoWell® Assay Plate, which contains 3,456 wells in a standard microplate footprint.

Ion Channel Platform. Our patented universal ion channel technology platform, which includes the VIPR subsystem, our proprietary voltage ion sensor probes and voltage ion probe reader, was first developed in 1997. This platform facilitates the rapid generation of screening assays and the high throughput screening of ion channel targets by optically measuring changes in membrane potential in live cells in an automated, microtiter plate format. The second generation, VIPR II subsystem is capable of screening in 96-well and 384-well microplate formats with a significant increase in throughput over the original VIPR subsystem. We are developing next-generation ion channel screening technology to facilitate drug discovery in this area.

Corporate Collaborations

We have entered into corporate collaborations with pharmaceutical companies that provide financial and other resources, including capabilities in research, development, manufacturing, and sales and marketing, to support our research and development programs. At present, we have the following major corporate collaborations:

Novartis Pharma AG

In May 2000 we entered into an agreement with Novartis Pharma AG to collaborate on the discovery, development and commercialization of small molecule drugs directed at targets in the kinase protein family. Under the agreement, Novartis agreed to pay us up to approximately \$600 million in pre-commercial payments, comprised of \$15 million paid upon signing of the agreement, up to \$200 million in product research funding over six years and up to approximately \$400 million in further license fees, milestone payments and cost reimbursements. These amounts are based on the

development of eight drug candidates. In addition, Novartis created a \$200 million loan facility to support certain clinical studies, which we may draw down in increments of up to \$25 million for each drug candidate. The loan is interest free and Novartis will forgive the full amount of any advances if Novartis accepts the drug candidate for development under our agreement. We will have the responsibility for drug discovery and clinical proof-of-concept testing of drug candidates. Novartis will have exclusive worldwide development, manufacturing and marketing rights to clinically and commercially relevant drug candidates that it accepts from us for development. We will receive royalties on any products that are marketed as part of the collaboration. Subject to certain conditions, we will have co-promotion rights in the United States and Europe. We will retain the rights to any intellectual property resulting from this collaboration. Novartis may terminate this agreement without cause after four years upon one year's written notice.

Taisho Pharmaceutical Co., Ltd.

In November 1999, we entered into a collaboration with Taisho covering the discovery, development, and commercialization of caspase inhibitors for the treatment of cerebrovascular, cardiovascular and neurodegenerative diseases. Taisho will have an option to obtain marketing rights in Japan and certain Far East markets for any compounds arising from the collaboration. Under the agreement, Taisho agreed to pay us up to \$43 million comprised of research funding and milestone payments, including \$4.5 million for prior research costs. These amounts are based on the development of two compounds. We will also receive royalties on future product sales, if any. In addition, Taisho will also pay for certain costs of developing compounds that emerge from the caspase research program.

Serono S.A.

In December 2000, we entered into a collaboration with Serono S.A. to discover, develop, and market caspase inhibitors. Under the terms of the agreement, we could receive up to \$95 million to support and expand our drug discovery activities in the caspase protein family, including milestone payments as drug candidates move through development. Under the terms of the agreement, we will receive a total of up to \$5 million in payments for prior research, and could also receive up to \$20 million in research funding over the next five years. We could also receive an additional \$70 million in milestone payments for the successful development and commercialization of more than one drug candidate. The two companies will share development costs. Vertex and Serono will establish a joint venture for the commercialization of products in North America, where we will share marketing rights and profits from the sale of caspase inhibitors. Serono will have exclusive rights to market caspase inhibitors in other territories, excluding Japan and certain other countries in the Far East, and will pay us for the supply of drug substance. Serono has the right to terminate the agreement without cause upon 90 days written notice, effective either at September 30, 2002 or September 30, 2004.

Aventis S.A.

In September 1999, we entered into an expanded agreement with Hoechst Marion Roussel (HMR) covering the development of pralnacasan. HMR and Rhone-Poulenc Rorer merged to form Aventis in December 1999. Aventis has an exclusive worldwide license to develop, manufacture and market pralnacasan, as well as an exclusive option for all other compounds discovered as part of the research collaboration between Vertex and HMR that ended in 1997. Aventis will fund the development of pralnacasan. We may co-promote the product in the United States and Europe and will receive royalties on global sales, if any. Under the agreement, Aventis agreed to pay us \$20 million for prior research costs, and \$62 million in milestone payments for successful development by Aventis of pralnacasan in rheumatoid arthritis, the first targeted indication, as well as similar milestone payments for each additional indication. Aventis has the right to terminate this agreement without cause upon six months' written notice.

Schering AG (Germany)

In August 1998, we entered into a collaboration with Schering AG covering the research, development and commercialization of novel, orally active neurophilin ligand compounds to promote nerve regeneration for the treatment of a number of neurological diseases. Vertex and Schering AG will have an equal role in management of neurophilin ligand research and product development. In North America, we will have manufacturing rights, and we will share equally with Schering AG in the marketing expenses and profits from commercialized compounds. In addition to having manufacturing rights in North America, we retain the option to manufacture bulk drug substance for sales in territories outside Europe, the Middle East and Africa. Schering AG will have the right to manufacture and market any commercialized compounds in Europe, the Middle East and Africa, and will pay us a royalty on any product sales. Under the terms of the agreement, Schering AG will pay us up to \$88 million, comprised of \$6 million paid upon signing in September 1998, up to \$22 million of product research funding over five years and \$60 million of development and commercialization milestone payments. Schering AG has the right to terminate the agreement without cause upon six months' written notice.

Kissei Pharmaceutical Co., Ltd.

HIV Protease Inhibitors. In April 1993, we entered into a collaboration with Kissei covering the development of amprenavir, our HIV protease inhibitor. Kissei has exclusive rights to develop and commercialize amprenavir in Japan and will pay us a royalty on sales. We are responsible for the manufacture of bulk product for Kissei. Under the collaborative agreement, Kissei agreed to pay us up to \$20 million, comprised of \$9.8 million of product research funding over three years, \$7 million of development and commercialization milestone payments and a \$3.2 million equity investment. We have received the full amount of research funding specified under the agreement.

p38 MAP Kinase. In September 1997, we entered into a collaboration with Kissei to identify and develop compounds that target p38 MAP kinase, including VX-745 and VX-702. We will collaborate with Kissei in the development and commercialization of novel, orally active p38 MAP kinase inhibitors as drugs for the treatment of inflammatory and neurological diseases. Kissei has exclusive rights to develop and commercialize these compounds in Japan and certain Southeast Asian countries and semi-exclusive rights in China, Taiwan and South Korea. We retain exclusive marketing rights in the United States, Canada, Europe, and the rest of the world. In addition, we will have the right to supply bulk drug material to Kissei for sale in its territory, and will receive royalties and drug supply payments on any product sales. Under the terms of the agreement, Kissei agreed to pay us up to \$22 million, comprised of a \$4 million license payment paid in September 1997, \$11 million of product research funding over three years and \$7 million of development and commercialization milestone payments. Additionally, Kissei agreed to pay certain costs. The research program ended on June 30, 2000, and we have received the full amount of research funding specified under the agreement. Kissei has the right to terminate the agreement without cause upon six months' notice.

Eli Lilly & Company

In June 1997, we entered into a collaboration with Eli Lilly covering the development of novel small molecule compounds to treat hepatitis C infection, including VX-950. Vertex and Eli Lilly will jointly manage the research, development, manufacturing and marketing of drug candidates emerging from the collaboration. We will have primary responsibility for drug design, process development and pre-commercial drug substance manufacturing, and Eli Lilly will have primary responsibility for formulation, preclinical and clinical development and global marketing. Vertex has retained options to assist with the promotion of drugs from the collaboration in the United States and other selected territories. We have the option to supply 100% of Eli Lilly's commercial drug substance supply needs. We will receive royalties on future product sales, if any. If we exercise our commercial supply option, we will receive drug supply payments, in addition. Under the terms of the agreement, Eli Lilly will pay us up to \$51 million, comprised of a \$3 million payment made in June 1997, \$33 million of product

research funding over six years and \$15 million of development and commercialization milestone payments. Eli Lilly has the right to terminate the agreement without cause upon six months' notice.

GlaxoSmithKline

In December 1993, we entered into a collaboration with GlaxoSmithKline covering the research, development and commercialization of HIV protease inhibitors, including Agenerase (amprenavir), its prodrug, VX-175 (also referred to as GW433908), and VX-385, a chemically distinct protease inhibitor. GlaxoSmithKline has exclusive rights to develop and commercialize our HIV protease inhibitors in all parts of the world except the Far East and pays us a royalty on sales. We have retained certain bulk drug manufacturing rights and certain co-promotion rights in the territories licensed to GlaxoSmithKline. Under the collaborative agreement, GlaxoSmithKline agreed to pay us up to \$42 million, comprised of a \$15 million license payment paid in 1993, \$14 million of product research funding over five years and \$13 million of development and commercialization milestone payments for an initial drug candidate. GlaxoSmithKline is also obligated to pay us additional development and commercialization milestone payments for subsequent drug candidates, including VX-175. We have received the full amount of research funding specified under the agreement. In addition, GlaxoSmithKline is required to bear the costs of development in its territory under the collaboration.

GlaxoSmithKline has the right to terminate its agreement with us without cause upon twelve months' notice. Termination of the agreement by GlaxoSmithKline will relieve it of its obligation to make further commercialization and development milestone and royalty payments, and will end any license granted to GlaxoSmithKline by us.

We and GlaxoSmithKline have a non-exclusive, worldwide license under certain Searle patent applications claiming HIV protease inhibitors, to permit Vertex and GlaxoSmithKline to develop, manufacture and market Agenerase free of the risk of intellectual property claims by Searle. The terms of the license require us to pay Searle a royalty on net sales.

Aurora Biosciences

Overview

We acquired Aurora Biosciences in July 2001. Aurora uses proprietary advances in biology, chemistry and automation to accelerate the discovery of new medicines. Aurora's core technologies include a broad portfolio of proprietary fluorescence assay technologies and screening platforms designed to provide an integrated solution for drug discovery. Its fluorescence assay technologies include GeneBLazer™, GenomeScreen™, Vivid™ and PhosphoryLIGHT™ technologies, as well as a broad collection of fluorescent proteins. Aurora's screening platforms include its ultra-high throughput screening system, the UHTSS® Platform, and its automated master compound store, the AMCS Platform, as well as its ion channel screening platform, which includes proprietary voltage sensor probes and voltage ion probe reader, the VIPR™ subsystem. Aurora also provides target discovery, assay development, screening and other services to its customers.

Aurora's technologies have been used by over 20 major life sciences companies and research organizations, including:

- Allergan
- American Home Products
- Bristol-Myers Squibb
- The Cystic Fibrosis Foundation
- Families of SMA
- F. Hoffmann-La Roche
- GlaxoSmithKline
- Genentech
- The Hereditary Disease Foundation
- Johnson & Johnson
- Merck & Co.
- NV Organon Laboratories
- Pfizer
- Pharmacia & Upjohn

A number of these organizations currently contract directly with Aurora for assay development, screening, target identification and other services. The agreements vary in duration and size and typically provide that Aurora will develop assays, deliver instrumentation, and provide ongoing scientific and technical support.

Technologies, Products and Services

Aurora focuses on the development and commercialization of technologies, products and services that provide solutions to bottlenecks in the drug discovery process. Aurora has developed and commercialized a broad range of technologies and products to facilitate drug discovery. Its technologies and products assist scientists by improving their ability to rapidly identify targets, develop assays and screen compounds to be used as potential new medicines.

Target Identification and Assay Development

- *GenomeScreen Technology.* Aurora uses its patented GenomeScreen technology to identify and validate targets by scanning the genome of living human cells and identifying those genes activated or repressed in disease states. GenomeScreen also facilitates the rapid development of cell-based assays for endogenously expressed targets, without having to utilize cloned cDNAs for those targets. Aurora has used this technology to generate hundreds of cell-based assays. In addition, Aurora has used GenomeScreen to assist in mapping gene activation and cell signaling pathways and characterizing poorly understood cellular processes.
- *GeneBLAzer Technology.* Aurora's patented GeneBLAzer technology enables scientists to rapidly develop cell-based assays with fluorescence-activated cell sorting (FACS). GeneBLAzer is readily adapted to a broad range of target classes, including G protein-coupled receptors (GPCRs), chemokine receptors, transcription factors and intracellular cis-acting proteases. Using GeneBLAzer, Aurora has developed over 150 assays relating to various therapeutic areas, including inflammation, oncology, metabolic, infectious and central nervous system diseases, for our collaborators and ourselves.
- *Fluorescence Polarization Technology.* Scientists use Aurora's fluorescence polarization technology to study molecular interactions in a number of drug discovery-related applications, including protein-DNA interactions, immunoassays, protease assays, epitope mapping, DNA hybridization and receptor-ligand binding studies. Aurora's fluorescence polarization technology includes its Beacon® fluorescence polarization system and a wide range of homogeneous, solution-based high-throughput screening assays.
- *Fluorescent Proteins.* Fluorescent proteins are widely used as research tools, with over 2,300 related publications to date. Drug discovery-related applications of Aurora's patented fluorescent proteins include various methods of functional genomics, high throughput screening assays and gene profiling to assess the potential toxicity of compounds. Aurora's issued patents on fluorescent proteins, which include over 400 claims, are directed toward nucleic acids encoding fluorescent proteins, the fluorescent proteins themselves, various fusion proteins and methods of use.
- *Universal G-Proteins.* Scientists can use Aurora's patented universal G-proteins to measure the activity of different kinds of receptors in living human cells and to identify the function of receptors without previously known function.
- *Vivid Fluorogenic Substrates.* Aurora's patented Vivid fluorogenic substrates are useful for the rapid assessment of individual compounds and compound libraries to determine whether they may have potentially unfavorable interactions with key metabolic enzymes known as cytochrome P450 isozymes. Currently, these unwanted characteristics are identified later in the drug development process, after significant investment has been made in chemistry and pharmacology research.

- *PhosphoryLIGHT Technology.* Aurora's PhosphoryLIGHT technology facilitates the development of assays to measure the activity of enzymes controlling cellular activity. These enzymes are significant therapeutic targets for a wide range of diseases, including cancer, inflammation, nervous system conditions and metabolic diseases.
- *CellSensor Technology.* Aurora uses its CellSensor technology to identify the function of novel biologics (such as orphan secreted proteins) and compounds.
- *LRET Technology.* Aurora uses its luminescent resonance energy transfer (LRET) technology to develop biochemical and cell-based assays that require time resolved readouts. Time resolved assay formats avoid many of the common artifacts found in standard fluorescence readouts.

Ion Channel Assay Development and High Throughput Screening

Aurora's patented ion channel technology platform, which includes the VIPR subsystem, its proprietary voltage sensor probes and voltage ion probe reader, was first released in 1997. This platform facilitates the rapid generation of screening assays and the high throughput screening of ion channel targets by optically measuring changes in membrane potential in live cells in an automated, microtiter plate format. In late 2000, Aurora began marketing its second-generation voltage ion probe reader, the VIPR II subsystem, which has increased functionality and higher screening capacity. The VIPR II subsystem is capable of screening in 96-well and 384-well microplate formats, with a significant increase in throughput over the original VIPR subsystem. Because Aurora's ion channel technology platform focuses on changes in membrane potential, it is a universal platform that is independent of the particular ion being transported by the target channel. It is applicable to the majority of ion channel families, including voltage-gated and ligand-gated potassium, sodium, calcium and chloride channels, as well as other types of channels. Using this patented functional assay and screening technology, Aurora has developed over 50 assays relating to therapeutic areas, including cardiovascular, metabolic and nervous system diseases, for our collaborators and ourselves.

Assay Development and Screening Services

Aurora provides assay development and screening services which generate revenue and also provide Aurora with valuable experience working with difficult drug targets.

Protein Manufacturing, Sales and Services

Aurora produces and sells proteins and provides protein cloning, expression and purification services through its subsidiary PanVera. Pan Vera has produced hundreds of recombinant proteins for commercial sale, focusing on protein families that are of broad interest from a therapeutic perspective, including nuclear receptors, protein kinases and drug metabolizing enzymes.

Intellectual Property

We vigorously pursue patents to protect our intellectual property. As of December 31, 2001, we had 150 issued U.S. patents and 186 pending U.S. patent applications covering proprietary technologies and intellectual property within our discovery and development programs, as well as foreign counterparts in many other countries. As of January 18, 2002, Aurora and its subsidiary PanVera owned or exclusively licensed 84 issued patents covering their technologies and had received notices of allowance with respect to five patent applications. Certain aspects of Aurora's fluorescent protein technology and ion channel technology are exclusively licensed from the Regents of the University of California.

We actively seek, when appropriate, protection for our products and proprietary information by means of United States and foreign patents, trademarks and contractual arrangements. In addition, we rely upon trade secrets and contractual arrangements to protect certain of our proprietary information and products. In addition to patents and pending patent applications that relate to potential drug

targets, compounds we are developing to modulate those targets, and methods of using those compounds, we have several patents and pending patent applications directed to proprietary elements of our drug discovery platform. These include a patent application on our SHAPES approach to NMR-based screening and on the use of a protein or a mutant of that protein to design inhibitors of other related proteins. We have also filed patent applications and obtained patents related to the three-dimensional atomic structures of targets of interest, the use of those structures to design drugs, classes of compounds that bind to a target of interest, and the interactions required between a compound and a target of interest.

Much of our technology and many of our processes depend upon the knowledge, experience and skills of key scientific and technical personnel. To protect our rights to our proprietary know-how and technology, we require all employees, consultants and advisors to enter into confidentiality agreements that prohibit the disclosure of Vertex confidential information to anyone outside Vertex. These agreements typically require disclosure and assignment to Vertex of ideas, developments, discoveries and inventions made by employees, consultants and advisors.

Patents and Pending Applications

We have issued patents and pending applications in the United States, and in foreign countries we deem appropriate, covering intellectual property developed as part of each of our most advanced research, development and commercialized programs. These include:

- issued United States patents that cover classes of chemical compounds, pharmaceutical formulations and/or uses of the same for treating HIV infection and AIDS. The patents include specific coverage for amprenavir, pharmaceutical formulations containing amprenavir and methods of using of amprenavir to treat HIV infection or AIDS-related central nervous system disorders. Another issued United States patent covers processes for preparing synthetic intermediates useful in the synthesis of a class of compounds that includes amprenavir. We have a non-exclusive, worldwide license under certain Searle patent applications claiming HIV protease inhibitors. We have applications pending in the United States and other countries claiming VX-175 and related compounds. We also have applications pending in the United States and other countries claiming VX-385 and related compounds.
- issued United States patents that cover classes of chemical compounds, pharmaceutical compositions containing such compounds, and methods of using those compounds to treat or prevent IMPDH-mediated diseases. The class of compounds covered by one of these patents includes merimepodib. We also have applications pending in the United States and other countries claiming VX-148, VX-944, and related compounds.
- issued United States patents claiming Incel and structurally related compounds, VX-853 and structurally related compounds, and other compounds for treating multidrug resistance, as part of our MDR research and development program.
- issued United States patents covering pralnacasan, the active metabolite of pralnacasan, and several different classes of compounds useful as inhibitors of ICE, as well as pharmaceutical compositions containing those compounds and methods of using those compounds to treat ICE-related diseases. These patents and applications also include a series of patents and applications purchased from Sanofi S.A., in July 1997. We also have a United States patent obtained from Sanofi S.A. that covers DNA sequences encoding ICE. We also have applications pending in the United States and other countries claiming VX-765 and related compounds.
- an issued patent that covers a class of chemical compounds that includes VX-745, as well as applications claiming VX-745 specifically, compositions comprising those compounds and the use of those compounds to treat p38-related disorders, as part of our p38 MAP kinase research and development program. We also have applications pending in the United States and other countries claiming VX-702, VX-850, and related compounds.

- issued United States patents covering various classes of chemical compounds and their use to treat a wide variety of neurological disorders.
- issued United States patents and pending applications covering assays useful to evaluate potential inhibitors of hepatitis C protease. We also have issued United States patents covering the X-ray crystal structures of hepatitis C protease and hepatitis C helicase, including the use of those structures to develop hepatitis C protease inhibitors and hepatitis C helicase inhibitors, respectively. Other issued United States patents and worldwide pending applications cover VX-950, additional hepatitis C protease inhibitors and hepatitis C helicase inhibitors.
- applications pending in the United States and other countries claiming VX-799 and related compounds. We also have filed applications claiming other classes of caspase inhibitors and a caspase target discovered under our caspase inhibitors program.
- issued United States patents claiming pharmaceutical compositions comprising VX-563 and related compounds, and methods of treating various diseases with such compositions.
- filed applications claiming inhibitors of multiple kinases, as part of our kinase research programs.
- filed applications and an issued United States patent for methods of designing novel chemical inhibitors of protein kinases. The patented method involves using mutagenesis techniques to create hybrid kinases that act as surrogate targets for drug design and compound screening. This method, which combines the disciplines of cell biology, structural genomics, computational chemistry and medicinal chemistry, may accelerate the design and development of new drug candidates by reducing lead discovery and optimization timelines.
- filed applications claiming inhibitors of bacterial gyrase.

We do not know whether any patents will issue from any of our patent applications or, even if patents issue or have issued, that the issued claims will provide us with any significant protection against competitive products or otherwise be valuable commercially. Legal standards relating to the validity of patents and the proper scope of their claims in the biopharmaceutical field are uncertain. We also cannot be sure that we will be able to avoid infringing, and thus having to negotiate a license under, any patents issued to others, or that a license to such patents would be available on commercially acceptable terms, if at all.

Manufacturing

We rely on third party manufacturers and collaborative partners to produce our compounds for preclinical and clinical purposes and may do so for commercial production of any compounds that are approved for marketing. Commercial manufacturing of Agenerase is being done by GlaxoSmithKline. We retain the option to manufacture a portion of GlaxoSmithKline's requirements for bulk drug substance for Agenerase and its prodrug, VX-175. If we were to exercise that option, we would rely upon one or more contract manufacturers to manufacture the bulk drug substance on our behalf.

We have established a quality assurance program, including a set of standard operating procedures, intended to ensure that third party manufacturers under contract produce our compounds in accordance with the FDA's current Good Manufacturing Practices, or cGMP, and other applicable regulations.

We believe that all of our existing compounds can be produced using established manufacturing methods, primarily through standard techniques of pharmaceutical synthesis. We believe that we will be able to continue to negotiate third party manufacturing arrangements on commercially reasonable terms and that it will not be necessary for us to develop internal manufacturing capability in order to successfully commercialize our products. Our objective is to maintain flexibility in deciding whether to develop internal manufacturing capabilities for certain of our potential products. However, in the event that we are unable to obtain contract manufacturing, or obtain such manufacturing on commercially

reasonable terms, we may not be able to commercialize our products as planned. We have limited experience in manufacturing pharmaceutical or other products or in conducting manufacturing testing programs required to obtain FDA and other regulatory approvals, and there can be no assurance that we will further develop such capabilities successfully.

Since most of our potential products are at an early stage of development, we will need to improve or modify our existing manufacturing processes and capabilities to produce commercial quantities of any drug product economically. We cannot quantify the time or expense that may ultimately be required to improve or modify our existing process technologies, but it is possible that such time or expense could be substantial.

The production of our compounds is based in part on technology that we believe to be proprietary. We may license this technology to contract manufacturers to enable them to manufacture compounds for us. In addition, a contract manufacturer may develop process technology related to the manufacture of our compounds that the manufacturer owns either independently or jointly with us. This would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have our products manufactured.

Aurora manufactures the UHTSS Platform, the AMCS Platform, the sample distribution system, and the VIPR and VIPR II at its facilities in San Diego, California, except certain components of the UHTSS Platform and AMCS Platform, which are purchased from Universal Technologies, Inc., and the enclosures for the UHTSS Platform and AMCS Platform, which are purchased from Environmental Specialties, Inc.

Competition

We are engaged in biopharmaceutical fields characterized by extensive research efforts, rapid technological progress and intense competition. There are many public and private companies, including pharmaceutical companies, chemical companies and biotechnology companies, engaged in developing products for the same human therapeutic applications as those that we are targeting. In order for us to compete successfully, we must demonstrate improved safety, efficacy, ease of manufacturing and market acceptance of our products over those of our competitors who have received regulatory approval and are currently marketing their drugs. In the field of HIV protease inhibition, Merck & Co., Inc., Abbott Laboratories, Inc., Hoffmann-La Roche, and Pfizer Inc. have other HIV protease inhibitor drugs on the market. Many of our competitors have substantially greater financial, technical and human resources than ours and more experience in the development of new drugs.

There are a number of companies that compete with Aurora in various aspects of its business. For instance, companies such as Cellomics, Discovery Partners International, Evotec and Molecular Devices develop and commercialize proprietary research tools, reagents, instruments and systems which compete with Aurora's proprietary screening platforms and reagents. There are also a number of companies such as Albany Molecular Research, ArQule, Array Biopharma, Cambridge Drug Discovery, Discovery Partners International, Oxford Asymmetry, Pharmacopeia and Tripos, that develop and commercialize compound libraries and use chemistry capabilities to test and screen potential drug candidates.

Government Regulation

Our development, manufacture and potential sale of therapeutics are subject to extensive regulation by United States and foreign governmental authorities. In particular, pharmaceutical products are subject to rigorous preclinical and clinical testing and to other approval requirements by the FDA in the United States under the Food, Drug and Cosmetic Act, and by comparable agencies in most foreign countries.

As an initial step in the FDA regulatory approval process, preclinical studies are typically conducted in animals to identify potential safety problems. For certain diseases, animal models exist that are believed to be predictive of human efficacy. For such diseases, a drug candidate is tested in an

animal model. The results of the studies are submitted to the FDA as a part of the Investigational New Drug application (IND) which is filed to comply with FDA regulations prior to commencement of human clinical testing in the U.S. For diseases for which no appropriately predictive animal model exists, no such results can be filed. For several of our drug candidates, no appropriately predictive model exists. As a result, no *in vivo* evidence of efficacy would be available until such compounds progress to human clinical trials.

Clinical trials are typically conducted in three sequential phases, although the phases may overlap. In Phase I, which frequently begins with the initial introduction of the drug into healthy human subjects prior to introduction into patients, the compound will be tested for safety, dosage tolerance, absorption, bioavailability, biodistribution, metabolism, excretion, clinical pharmacology and, if possible, for early information on effectiveness. Phase II typically involves studies in a small sample of the intended patient population to assess the efficacy and duration of the drug for a specific indication, to determine dose tolerance and the optimal dose range and to gather additional information relating to safety and potential adverse effects. Phase III trials are undertaken to further evaluate clinical safety and efficacy in an expanded patient population at geographically dispersed study sites, to determine the overall risk-benefit ratio of the drug and to provide an adequate basis for physician labeling. Each trial is conducted in accordance with certain standards under protocols that detail the objectives of the study, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND. Further, each clinical study must be evaluated by an independent Institutional Review Board at the institution at which the study will be conducted. The Institutional Review Board will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution.

Data from preclinical testing and clinical trials are submitted to the FDA in a New Drug Application (NDA) for marketing approval. The process of completing clinical testing and obtaining FDA approval for a new drug is likely to take a number of years and require the expenditure of substantial resources. Preparing an NDA involves considerable data collection, verification, analysis and expense, and there can be no assurance that approval will be granted on a timely basis, if at all. The approval process is affected by a number of factors, including the severity of the disease, the availability of alternative treatments and the risks and benefits demonstrated in clinical trials. The FDA may deny an NDA if applicable regulatory criteria are not satisfied or may require additional testing or information. Among the conditions for marketing approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform to the FDA's cGMP regulations, which must be followed at all times. In complying with standards set forth in these regulations, manufacturers must continue to expend time, monies and effort in the area of production and quality control to ensure full technical compliance. Manufacturing establishments, both foreign and domestic, also are subject to inspections by or under the authority of the FDA and by or under the authority of other federal, state or local agencies.

Even after initial FDA approval has been obtained, further studies, including post-marketing studies, may be required to provide additional data on safety and will be required to gain approval for the use of a product as a treatment for clinical indications other than those for which the product was initially tested. Also, the FDA will require post-marketing reporting to monitor the side effects of the drug. Results of post-marketing programs may limit or expand further marketing of the drug products. Further, if there are any modifications to the drug, including changes in indication, manufacturing process, labeling or manufacturing facilities, an NDA supplement may be required to be submitted to the FDA.

The Orphan Drug Act provides incentives to drug manufacturers to develop and manufacture drugs for the treatment of diseases or conditions that affect fewer than 200,000 individuals in the United States. Orphan drug status can also be sought for diseases or conditions that affect more than 200,000 individuals in the United States if the sponsor does not realistically anticipate its product becoming profitable from sales in the United States. Under the Orphan Drug Act, a manufacturer of a designated orphan product can seek tax benefits, and the holder of the first FDA approval of a

designated orphan product will be granted a seven-year period of marketing exclusivity for that product for the orphan indication. While the marketing exclusivity of an orphan drug would prevent other sponsors from obtaining approval of the same compound for the same indication, it would not prevent other types of drugs from being approved for the same use. We may apply for orphan drug status for certain indications of MDR in cancer.

Under the Drug Price Competition and Patent Term Restoration Act of 1984, a sponsor may be granted marketing exclusivity for a period of time following FDA approval of certain drug applications if FDA approval is received before the expiration of the patent's original term. This marketing exclusivity would prevent a third party from obtaining FDA approval for a similar or identical drug through an Abbreviated New Drug Application, which is the application form typically used by manufacturers seeking approval of a generic drug. The statute also allows a patent owner to extend the term of the patent for a period equal to one-half the period of time elapsed between the filing of an IND and the filing of the corresponding NDA plus the period of time between the filing of the NDA and FDA approval. We intend to seek the benefits of this statute, but there can be no assurance that we will be able to obtain any such benefits.

Whether or not FDA approval has been obtained, approval of a drug product by regulatory authorities in foreign countries must be obtained prior to the commencement of commercial sales of the product in such countries. Historically, the requirements governing the conduct of clinical trials and product approvals, and the time required for approval, have varied widely from country to country.

In addition to the statutes and regulations described above, we are also subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and other present and potential future federal, state and local regulations.

Employees

As of December 31, 2001, we had more than 1,000 employees, including approximately 570 in research and development, 260 in support services and 161 in general and administrative functions. Approximately 66 of these employees were located at our U.K. research and development facility, 103 of these employees were located at our PanVera facility in Madison, Wisconsin, and 350 of these employees were located at our facility in San Diego (including Aurora). Our scientific staff members (246 of whom hold Ph.D. and/or M.D. degrees, including 52 at Aurora and PanVera) have diversified experience and expertise in molecular and cell biology, biochemistry, animal pharmacology, synthetic organic chemistry, protein X-ray crystallography, protein nuclear magnetic resonance spectroscopy, computational chemistry, biophysical chemistry, medicinal chemistry, clinical pharmacology and clinical medicine. Our employees are not covered by a collective bargaining agreement, and we consider our relations with our employees to be good.

EXECUTIVE OFFICERS AND DIRECTORS

The names, ages and positions held by our executive officers and directors are as follows:

<u>Name</u>	<u>Age</u>	<u>Position</u>
Joshua S. Boger, Ph.D.	50	Chairman and Chief Executive Officer
Vicki L. Sato, Ph.D.	54	President
John J. Alam, M.D.	40	Senior Vice President of Drug Evaluation and Approval
Lynne H. Brum	38	Vice President of Corporate Development and Communications
Iain P. M. Buchanan	48	Vice President of European Operations; Managing Director of Vertex Pharmaceuticals (Europe) Limited
Kenneth S. Boger	55	Senior Vice President and General Counsel
N. Anthony Coles, M.D.	41	Senior Vice President, Commercial Operations-Pharmaceutical Products
Ian F. Smith	36	Vice-President and Chief Financial Officer
Michael G. Wokasch	50	President, Aurora Biosciences and PanVera Corporation
Barry M. Bloom, Ph.D.	73	Director
Roger W. Brimblecombe, Ph.D., D.Sc.	72	Director
Stuart J. Collinson, Ph.D.	42	Director
Donald R. Conklin	65	Director
Bruce I. Sachs	42	Director
Charles A. Sanders, M.D.	70	Director
Elaine S. Ullian	54	Director

All executive officers are elected by the Board of Directors to serve in their respective capacities until their successors are elected and qualified or until their earlier resignation or removal.

Dr. Joshua Boger is a founder of Vertex. He has been Chief Executive Officer since 1992 and Chairman of the Board since 1997. He was our President from our inception in 1989 until December 2000, and Chief Scientific Officer from 1989 until May 1992. Dr. Boger has been a director since Vertex's inception. Prior to founding Vertex in 1989, Dr. Boger held the position of Senior Director of Basic Chemistry at Merck Sharp & Dohme Research Laboratories in Rahway, New Jersey, where he headed both the Department of Medicinal Chemistry of Immunology & Inflammation and the Department of Biophysical Chemistry. Dr. Boger holds a B.A. in chemistry and philosophy from Wesleyan University and M.S. and Ph.D. degrees in chemistry from Harvard University. Dr. Boger is the brother of Mr. Kenneth Boger, the Company's Senior Vice President and General Counsel.

Dr. Sato joined Vertex in September 1992 as Vice President of Research and Chief Scientific Officer. She was appointed Senior Vice President of Research and Development in September 1994 and became President of Vertex in December 2000. She served as Chair of the Scientific Advisory Board from 1992 until December 2000. Previously, she was Vice President, Research and a member of the Scientific Board of Biogen, Inc. As research head at Biogen, she directed research programs in the fields of inflammation, immunology, AIDS therapy and cardiovascular therapy from early research into

advanced product development. Dr. Sato received an A.B. in biology from Radcliffe College and A.M. and Ph.D. degrees from Harvard University. Following postdoctoral work in chemistry and immunology at the University of California at Berkeley and Stanford Medical School, she was appointed to the faculty of Harvard University in the Department of Biology.

Dr. Alam served as Vice President of Clinical Development of the Company from October 1997 until January 2001, when he was appointed Senior Vice President of Drug Evaluation and Approval. Dr. Alam came to Vertex from Biogen, Inc., where he held a variety of positions from 1991-1997, including Director of Medical Research and Program Executive for Avonex (beta interferon). Prior to joining Biogen, Dr. Alam was a Research Fellow at the Dana Farber Cancer Institute and had completed an internal medicine residency at The Brigham and Women's Hospital in Boston. Dr. Alam holds an M.D. from Northwestern University Medical School and a S.B. in Chemical Engineering from the Massachusetts Institute of Technology.

Ms. Brum joined Vertex as Director, Corporate Communications in 1994 and was Vice President of Corporate Communications of the Company from 1998 until January 2001, when she was appointed Vice President of Corporate Communications and Market Development. Ms. Brum came to Vertex from Feinstein Kean Healthcare, a communications and business consulting practice, where she was a vice president. Previously, she held corporate communications and research positions at Biogen, Inc. Ms. Brum holds an M.B.A. from the Simmons Graduate School of Management, and a B.A. in biological sciences from Wellesley College.

Mr. Buchanan joined Vertex in April 1994 from Cilag AG, a subsidiary of Johnson & Johnson based in Zug, Switzerland, where he served as its Regional Licensing Director since 1987. He previously held the position of Marketing Director of Biogen, Inc. in Switzerland. Prior to Biogen, Mr. Buchanan served in Product Management at Merck Sharp & Dohme (UK) Limited. Mr. Buchanan holds a B.Sc. from the University of St. Andrews, Scotland.

Mr. Kenneth Boger joined Vertex as Senior Vice President and General Counsel in October 2001. He came to Vertex from the law firm of Kirkpatrick & Lockhart, where he was a partner specializing in business and corporate law and was a member of the firm's Management Committee. Prior to the merger of Kirkpatrick & Lockhart with the Boston law firm of Warner & Stackpole in 1999, Mr. Boger was a partner at Warner & Stackpole, where he served on the Executive Committee from 1988 to 1997. Mr. Boger holds a B.A. in history from Duke University, an MBA from the Graduate School of Business at the University of Chicago, and a J.D. from Boston College Law School. Mr. Boger is the brother of Dr. Joshua Boger, the Company's Chairman and Chief Executive Officer.

Dr. Coles joined Vertex as Senior Vice President, Commercial Operations—Pharmaceutical Products in March, 2002. He came to Vertex from Bristol-Myers Squibb, where he served in a variety of positions since joining BMS in 1996, including Senior Vice President of Strategy and Policy, Senior Vice President, Marketing and Medical Affairs for the Neuroscience, Infectious Disease, and Dermatology Division, and Vice President, West Area Sales—Cardiovascular and Metabolic Business Unit for U.S. Primary Care. Prior to joining BMS, Dr. Coles was Vice-President of the Hypertension and Heart Failure Business Group at Merck. Dr. Coles holds an M.D. degree from Duke University, a Masters Degree in Public Health from Harvard University and a B.S. degree from Johns Hopkins University.

Mr. Smith joined Vertex as Vice President and Chief Financial Officer in October 2001. He came to Vertex from Ernst & Young, LLP, an accounting firm, where he had served as a partner in their Life Science and Technology Practice since 1999. He had various responsibilities in the accounting, auditing and mergers and acquisitions groups. Mr. Smith initially joined Ernst & Young's U.K. firm in 1987, and then joined their Boston office in 1995. Mr. Smith holds a B.A. in Accounting and Finance from Manchester Metropolitan University, U.K., is a member of the American Institute of Certified Public Accountants and is a Chartered Accountant of England and Wales.

Mr. Wokasch joined PanVera in July 2001 and currently serves as President of PanVera and, effective March 2002, as President of Aurora. Prior to joining PanVera, Mr. Wokasch served as Chief Executive Officer and President of Gala Design, Inc. Prior to Gala Design, he served as Vice President, Marketing and Sales, at Promega Corporation. From 1997 to 1999, he was Senior Vice President and Group President at Covance. Prior to 1997, Mr. Wokasch held various management positions at Abbott Laboratories, as well as sales and marketing positions at Merck & Co., Inc. He obtained his Bachelor of Science degree in Pharmacy from the University of Minnesota.

Dr. Bloom has served as our director since 1994. He was formerly with Pfizer Inc., as Executive Vice President of Research and Development from 1992 to 1993, as Vice President from 1990 to 1992, and as a director from 1973 to 1993. He also serves as a director of Cubist Pharmaceuticals Inc., Incyte Genomics Inc., Neurogen Corporation and Microbia.

Dr. Brimblecombe has served as our director since 1993. He served as Chairman of Vanguard Medica Ltd. from 1991 to 2000, as Chairman of Core Group plc since 1997, and as Non-Executive Chairman of Oxford Asymmetry International plc from 1997 to 2000. From 1979 to 1990, he held various Vice Presidential posts in SmithKline & French Laboratories' research and development organization. He also serves as a director of several companies located in Europe.

Dr. Collinson joined us as a member of the Board of Directors in July 2001. He currently serves as a Partner at Forward Ventures. Prior to our merger with Aurora in 2001, Dr. Collinson served as the President, Chief Executive Officer and Chairman of the Board of Aurora. Before joining Aurora, Dr. Collinson served as a consultant to Aurora from December 1998 to May 1999 and as Chief Executive Officer of Andaris, Ltd., a privately held biopharmaceutical company, from June 1998 to November 1998. Prior to Andaris, Dr. Collinson held senior management positions with Glaxo Wellcome from December 1994 through June 1998, most recently serving as Co-Chairman, Hospital and Critical Care Therapy Management Team and Director of Hospital and Critical Care. Dr. Collinson received his Ph.D. in physical chemistry from the University of Oxford, England and his M.B.A. from Harvard University.

Mr. Conklin has served as our director since 1994. He served as Executive Vice President of Schering Plough from 1986 to 1996, when he retired. He also serves as a director of AlfaCell Inc. and Ventiv Inc.

Mr. Sachs has served as our director since 1998. He currently serves as a General Partner at Charles River Ventures. From 1998 to 1999, he served as Executive Vice President and General Manager of Ascend Communications, Inc. From 1997 until 1998, Mr. Sachs served as President and CEO of Stratus Computer, Inc. From 1995 to 1997, he served as Executive Vice President and General Manager of the Internet Telecom Business Group at Bay Networks, Inc. From 1993 to 1995, he served as President and Chief Executive Officer at Xylogics, Inc.

Dr. Sanders has served as our director since 1996. He retired in 1994 as Chief Executive Officer and in 1995 as Chairman of Glaxo Inc. From 1990 to 1995, he served as a member of the board of Glaxo plc. From 1981 to 1989, Dr. Sanders held a number of positions at the Squibb Corporation, including that of Vice Chairman. Dr. Sanders has served on the boards of Merrill Lynch, Reynolds Metals Co. and Morton International Inc. He is currently a director of Biopure Corporation, Edgewater Inc., Genentech, Inc., Genaera Pharmaceuticals Inc., Pharmacopeia Inc., Scios, Inc., and Trimeris Inc.

Ms. Ullian has served as our director since 1997. Since 1996, she has served as President and Chief Executive Officer of Boston Medical Center. From 1994 to 1996, she served as President and Chief Executive Officer of Boston University Medical Center Hospital. From 1987 to 1994, Ms. Ullian served as President and Chief Executive Officer of Faulkner Hospital. She also serves as a director of Hologic Inc.

SCIENTIFIC ADVISORY BOARD

Vertex's Scientific Advisory Board consists of individuals with demonstrated expertise in various fields who advise us concerning long-term scientific planning, research and development. The Scientific Advisory Board also evaluates our research programs, recommends personnel to us and advises us on technological matters. The members of the Scientific Advisory Board, which is chaired by Dr. Mark Murcko, our Chief Technology Officer, are:

- Mark Murcko, Ph.D. Vice President and Chief Technology Officer, Vertex Pharmaceuticals Incorporated.
- Vicki L. Sato, Ph.D. President, Vertex Pharmaceuticals Incorporated.
- Steven J. Burakoff, M.D. Laura and Isaac Perlmutter Professor, New York University School of Medicine; Director, New York University Cancer Institute; Director, Skirball Institute of Biomolecular Medicine.
- Eugene H. Cordes, Ph.D. Professor of Medicinal Chemistry, College of Pharmacy and Adjunct Professor of Chemistry, College of Literature, Science and the Arts, University of Michigan, Ann Arbor.
- Stephen C. Harrison, Ph.D. Higgins Professor of Biochemistry, Harvard University; Investigator, Howard Hughes Medical Institute; Professor of Biological Chemistry and Molecular Pharmacology and Professor of Pediatrics, Harvard Medical School.
- Jeremy R. Knowles, D. Phil. Dean of the Faculty of Art and Sciences, and Amory Houghton Professor of Chemistry and Biochemistry, Harvard University.
- Robert T. Schooley, M.D. Tim Gill Professor of Medicine and Head of the Division of Infectious Disease, University of Colorado Health Sciences Center.
- Dr. Roger Tsien, Ph.D. Investigator, Howard Hughes Medical Institute; Professor of Pharmacology and Professor of Chemistry and Biochemistry, University of California, San Diego.

Other than Dr. Murcko and Dr. Sato, none of the members of the Scientific Advisory Board is employed by Vertex, and members may have other commitments to or consulting or advisory contracts with their employers or other entities that may conflict or compete with their obligations to us. Accordingly, such persons are expected to devote only a small portion of their time to us. In addition to our Scientific Advisory Board, we have established consulting relationships with a number of scientific and medical experts who advise us on a project-specific basis.

RISK FACTORS

WE DO NOT KNOW HOW SUCCESSFUL AGENERASE WILL BE IN EUROPE, OR WHETHER U.S. AGENERASE SALES WILL CONTINUE AT CURRENT LEVELS.

Agenerase's share of the worldwide protease inhibitor market may decrease due to competitive forces and market dynamics. Six other HIV protease inhibitors and a number of other products, including Gilead's Viread, DuPont's Sustiva and GlaxoSmithKline's Ziagen, are on the market for the treatment of HIV infection and AIDS. Other drugs are still in development by our competitors, including Bristol Myers Squibb and Boehringer Ingelheim, which may have better efficacy, fewer side effects, easier administration and/or lower costs than Agenerase. Moreover, the growth in the worldwide market for HIV protease inhibitors has, to a certain extent, occurred as a result of early and aggressive treatment of HIV infection with a protease inhibitor-based regimen. Changes in treatment strategy, in which treatment is initiated later in the course of infection, or in which treatment is more often initiated with a regimen that does not include a protease inhibitor, may result in less use of HIV protease inhibitors. In addition, the clinical benefit of strategies used by clinicians to boost drug levels of Agenerase by co-administering other antiretrovirals may not prove to be effective, or may not result in increased revenues. As a result, the total market for protease inhibitors, in the U.S. and Europe, may decline, decreasing Agenerase sales potential. Further, although we co-promote Agenerase in the

U.S. and Europe, GlaxoSmithKline is making most of the marketing and sales efforts and we will have little control over the success of those efforts. GlaxoSmithKline has the right to terminate its agreement with us without cause upon twelve months' notice.

IF WE DO NOT SUCCESSFULLY DEVELOP OUR DRUG PIPELINE, WE MAY NOT GENERATE SUFFICIENT FUNDS TO ACHIEVE OR SUSTAIN PROFITABILITY IN THE FUTURE.

As of December 31, 2001, our collaborators and we were conducting clinical development of six product candidates resulting from our research and development programs, including additional clinical trials of VX-175, merimepodib, pralnacasan and VX-148, and preclinical testing of eight product candidates from these programs. All of the products that we are pursuing will require extensive additional development, testing and investment, as well as regulatory approvals, prior to commercialization. Our product research and development efforts may not be successful. Our drug candidates may not enter preclinical or clinical studies as or when anticipated or receive the required regulatory approvals. Moreover, our products, if introduced, may not be commercially successful. The results of preclinical and initial clinical trials of products under development by us are not necessarily predictive of results that will be obtained from large-scale clinical testing. Clinical trials of products under development may not demonstrate the safety and efficacy of such products or result in a marketable product. In addition, the administration alone or in combination with other drugs of any product developed by us may produce undesirable side effects in humans.

The failure to demonstrate adequately the safety and efficacy of a therapeutic drug under development could delay or prevent regulatory approval of the product and could have a material adverse effect on our company. In addition, the FDA may require additional clinical trials, which could result in increased costs and significant development delays. While all or a portion of these additional costs may be covered by payments under our collaborative agreements, we bear all of the costs for our development candidates that are not partnered.

IF DELAYS IN PATIENT ENROLLMENT SLOW OUR DEVELOPMENT PROCESS WE MAY LOSE OUR COMPETITIVE ADVANTAGE OR BE UNABLE TO BRING OUR DRUGS TO MARKET.

The rate of completion of clinical trials of our products is dependent upon, among other factors, the rate of patient accrual. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the level of compliance by the clinical sites to clinical trial protocols, and the availability of clinical trial material. Delays in patient enrollment in clinical trials may result in increased costs, program delays or both, which could have a material adverse effect on our company. While all or a portion of these additional costs may be covered by payments under our collaborative agreements, we bear all of the costs for our development candidates that are not partnered. If our clinical trials are not completed, we may not be able to submit a new drug application and any such application may not be reviewed and approved by the FDA in a timely manner, if at all.

IF WE DO NOT OBTAIN REGULATORY APPROVAL FOR OUR PRODUCTS ON A TIMELY BASIS, OR AT ALL, OUR REVENUES WILL BE NEGATIVELY IMPACTED.

The FDA and comparable agencies in foreign countries impose substantial requirements on the introduction of therapeutic pharmaceutical products through lengthy and detailed laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures. Satisfaction of these requirements typically takes several years or longer and may vary substantially based upon the type, complexity and novelty of the pharmaceutical product. Data obtained from preclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. In addition, delays or rejections may be encountered based on changes in, or additions to, regulatory policies for drug approval during the period of product development and regulatory review. The effect of government regulation may be to delay or prevent the commencement of planned clinical trials for our drug candidates in clinical development, including VX-175,

merimepodib, pralnacasan, and VX-148. It may also delay the commercialization of our products; if any are developed and submitted for approval, for a considerable period of time, impose costly procedures upon our activities and provide competitive advantages to companies more experienced in regulatory affairs that compete with us. Moreover, even if approval is granted, such approval may entail limitations on the indicated uses for which a compound may be marketed.

IF WE ARE UNABLE TO ATTRACT AND RETAIN COLLABORATIVE PARTNERS FOR RESEARCH SUPPORT AND THE DEVELOPMENT AND COMMERCIALIZATION OF OUR PRODUCTS, WE MAY NOT BE ABLE TO FUND OUR RESEARCH AND DEVELOPMENT ACTIVITIES.

Our collaborative partners have agreed to fund portions of our research and development programs and/or to conduct certain research and development relating to specified products. In exchange, we have given them technology, product and marketing rights relating to those products. Some of our corporate partners, including Novartis, GlaxoSmithKline, Aventis and Eli Lilly, have rights to control the planning and execution of product development and clinical programs. The corporate partners may exercise their control rights in ways that may negatively impact the timing and success of those programs. Our collaborations are subject to termination rights by the collaborators. If any of Novartis, GlaxoSmithKline, Aventis or Eli Lilly were to terminate its relationship with us, or fail to meet its contractual obligations, it could have a material adverse effect on our ability to undertake research, to fund related and other programs and to develop, manufacture and market any products that may have resulted from the collaboration. For example, if Novartis were to terminate its collaboration with us before the end of the research term specified in the contract, we would no longer be eligible to receive milestone payments and reimbursements worth as much as \$600 million from Novartis. We expect to seek additional collaborative arrangements to provide research support and to develop and commercialize our products in the future. We may not be able to establish acceptable collaborative arrangements in the future and even if we establish such collaborations, they may not be successful. Under certain of our collaborative agreements, our collaborators have agreed to provide funding for only a portion of our research and development activities and we are committed to investing our own capital to fund the remainder of the agreed upon programs. However, we may not have adequate financial resources to satisfy those requirements.

IF WE LOSE OUR TECHNOLOGICAL ADVANTAGES, WE MAY NOT BE ABLE TO COMPETE IN THE MARKETPLACE.

We believe that our chemogenomics platform and parallel drug design strategy give us a technological advantage. However, the pharmaceutical research field is characterized by rapid technological progress and intense competition. As a result, we may not realize the expected benefits from these technologies. For example, a large pharmaceutical company, with significantly more resources than we have, could pursue a novel, systematic approach to discover drugs based on gene families using proprietary drug targets, compound libraries, compound approaches, structural protein analysis and information technologies. Such a company might identify broadly applicable compound classes faster and more effectively than we do, impeding our ability to develop and market drugs based on our approach. Further, we believe that interest in the application of structure-based drug design, parallel drug design and related approaches may continue and may accelerate as the strategies become more widely understood. Businesses, academic institutions, governmental agencies and other public and private research organizations are conducting research to develop technologies that may compete with those we use. It is possible that our competitors could acquire or develop technologies that would render our technology obsolete or noncompetitive. For example, a competitor could develop information technologies that accelerate the atomic-level analysis of potential compounds that bind to the active site of a drug target, and predict the absorption, toxicity, and relative ease-of-synthesis of candidate compounds. If we were unable to access the same technologies at an acceptable price, our business could be adversely affected.

IF OUR COMPETITORS BRING SUPERIOR PRODUCTS TO MARKET OR BRING THEIR PRODUCTS TO MARKET BEFORE WE DO, WE MAY BE UNABLE TO FIND A MARKET FOR OUR PRODUCTS.

Our products in development may not be able to compete effectively with products which are currently on the market or new products that may be developed by others. There are many other companies developing products for the same indications that we are pursuing in development. For example, we know of at least 10 drugs in development for HIV, 5 drugs in development for the treatment of hepatitis C infection, and 20 drugs in development for the treatment of rheumatoid arthritis, by competitors in the pharmaceutical and biotechnology industries. In order to compete successfully in these areas, we must demonstrate improved safety, efficacy, ease of manufacturing and gain market acceptance over competing products which have received regulatory approval and are currently marketed. Many of our competitors, including major pharmaceutical companies such as GlaxoSmithKline, Novartis, Abbott and Merck, have substantially greater financial, technical and human resources than we do. In addition, many of our competitors have significantly greater experience than we do in conducting preclinical testing and human clinical trials of new pharmaceutical products, and in obtaining FDA and other regulatory approvals of products. Accordingly, our competitors may succeed in obtaining regulatory approval for products more rapidly than we do. If we obtain regulatory approval and launch commercial sales of our products, we will also compete with respect to manufacturing efficiency and sales and marketing capabilities, areas in which we currently have limited experience.

THE LOSS OF THE SERVICES OF KEY EMPLOYEES OR THE FAILURE TO HIRE QUALIFIED EMPLOYEES WOULD NEGATIVELY IMPACT OUR BUSINESS AND FUTURE GROWTH.

Because our products are highly technical in nature, we require the services of highly qualified and trained scientists who have the necessary skills to develop our products. Our future success will depend in large part on the continued services of our key scientific and management personnel, including Dr. Joshua S. Boger, our Chief Executive Officer, and Dr. Vicki L. Sato, our President. While we have entered into employment agreements with Dr. Boger and Dr. Sato, they may be terminated by the employee upon six months' notice.

We face intense competition for our scientific personnel from our competitors, our collaborative partners and other companies throughout our industry. Moreover, the growth of local biotechnology companies and the expansion of major pharmaceutical companies into the Cambridge area has increased competition for the available pool of skilled employees, especially in technical fields, and the high cost of living in the Boston area makes it difficult to attract employees from other parts of the country. A failure to retain, as well as hire, train and effectively integrate into our organization, a sufficient number of qualified scientists and professionals would negatively impact our business and our ability to grow our business. In addition, the level of funding under certain of our collaborative agreements, in particular the Novartis collaboration, depends on the number of our scientists performing research under those agreements. If we cannot hire and retain the required personnel, funding received under the agreements may be reduced.

IF WE FAIL TO MANAGE OUR GROWTH EFFECTIVELY, OUR BUSINESS MAY SUFFER.

During the year 2001, we added approximately 96 employees, increasing the size of our organization by almost 21%, exclusive of approximately 450 employees who came to us through our acquisition of Aurora, and we intend to continue to grow. This growth, including growth resulting from the Aurora acquisition, requires a significant investment in personnel, management systems and resources. Our ability to commercialize our products, achieve our research and development objectives, and satisfy our commitments under our collaboration agreements depends on our ability to respond effectively to these demands and expand our internal organization to accommodate additional anticipated growth. If we are unable to manage our growth effectively, there could be a material adverse effect on our business.

WE DEPEND ON THIRD PARTY MANUFACTURERS, AND IF WE ARE UNABLE TO OBTAIN CONTRACT MANUFACTURING ON REASONABLE TERMS, WE MAY NOT BE ABLE TO DEVELOP OR COMMERCIALIZE OUR PRODUCTS.

Our ability to conduct clinical trials and our ability to commercialize our potential products will depend, in part, on our ability to manufacture our products on a large scale, either directly or through third parties, at a competitive cost and in accordance with FDA and other regulatory requirements. We have no experience in manufacturing pharmaceuticals or other products, and we may not be able to develop such capabilities in the foreseeable future. In addition, some of our current corporate partners have manufacturing rights with respect to our products under development. We are, therefore, dependent on third party manufacturers and our collaborative partners for the production of our compounds for preclinical research, clinical trial purposes and commercial production. Accordingly, if we are not able to obtain contract manufacturing from these third parties on commercially reasonable terms, we may not be able to conduct or complete clinical trials or commercialize our products as planned. Further, commercial formulation and manufacturing processes have yet to be developed for our drug candidates other than Agenerase. As a result, our collaborators or we may encounter difficulties developing commercial formulations and manufacturing processes for our drug candidates that could result in delays in clinical trials, regulatory submissions, regulatory approvals and commercialization of our products.

IF OUR PATENTS DO NOT PROTECT OUR PRODUCTS, OR OUR PRODUCTS INFRINGE THIRD-PARTY PATENTS, WE COULD BE SUBJECT TO LITIGATION AND SUBSTANTIAL LIABILITIES.

As of December 31, 2001, we had 186 patent applications pending in the United States, as well as foreign counterparts in other countries. Our success will depend, in significant part, on our ability to obtain and maintain United States and foreign patent protection for our products, their uses and our processes to preserve our trade secrets and to operate without infringing the proprietary rights of third parties. We do not know whether any patents will issue from any of our patent applications or, even if patents issue or have issued, that the issued claims will provide us with any significant protection against competitive products or otherwise be valuable commercially. Legal standards relating to the validity of patents and the proper scope of their claims in the biopharmaceutical field are still evolving, and there is no consistent law or policy regarding the valid breadth of claims in biopharmaceutical patents or the effect of prior art on them. If we are not able to obtain adequate patent protection, our ability to prevent competitors from making, using and selling competing products will be limited. Furthermore, our activities may infringe the claims of patents held by third parties. We are currently contesting a suit filed by Chiron Corporation claiming infringement of three U.S. patents issued to Chiron, and a suit filed by Oregon Health Sciences University claiming part ownership of five of our neurophilia patents. Although we believe that the ultimate outcome of these actions will not have a material impact on our consolidated financial position, defense and prosecution of claims such as those at issue in the Chiron and Oregon Health Sciences University cases, as well as participation in other inter-party proceedings, can be expensive and time-consuming, even in those instances in which the outcome is favorable to us. If the outcome of any such litigation or proceeding were adverse, we could be subject to significant liabilities to third parties, could be required to obtain licenses from third parties or could be required to cease sales of affected products, any of which could have a material adverse effect on our consolidated financial position.

WE EXPECT TO INCUR FUTURE LOSSES AND WE MAY NEVER BECOME PROFITABLE.

We have incurred significant operating losses each year since our inception and expect to incur a significant operating loss in 2002. We believe that operating losses will continue beyond 2002, even if we receive significant future payments under our existing and future collaborative agreements and royalties on Agenerase sales, because we are planning to make significant investments in research and development, and will incur significant selling, general, and administrative expenses for our potential

products. We expect that losses will fluctuate from quarter to quarter and year to year, and that such fluctuations may be substantial. We may never achieve or sustain profitability.

WE MAY NEED TO RAISE ADDITIONAL CAPITAL THAT MAY NOT BE AVAILABLE.

We expect to incur substantial research and development and related supporting expenses as we design and develop existing and future compounds and undertake clinical trials of potential drugs resulting from such compounds. We also expect to incur substantial administrative and commercialization expenditures in the future and substantial expenses related to the filing, prosecution, defense and enforcement of patent and other intellectual property claims. We anticipate that we will finance these substantial cash needs with:

- future payments under our existing collaborative agreements;
- payments under new collaborative agreements;
- Agenerase royalty revenue;
- existing cash reserves, together with interest earned on those reserves;
- facilities and equipment financing; and
- future product sales to the extent that we market products directly.

We expect that funds from these sources will be sufficient to fund our planned activities for at least the next 18 months. If not, it will be necessary to raise additional funds through public offerings or private placements of equity or debt securities or other methods of financing. Any equity financings could result in dilution to our then-existing securityholders. Any debt financing, if available at all, may be on terms which, among other things, restrict our ability to pay dividends and interest (although we do not intend to pay dividends for the foreseeable future). The required interest payments associated with any significant additional debt financing could materially adversely impact our ability to service our convertible subordinated notes. The terms of any additional debt financing may also, under certain circumstances, restrict or prohibit us from making interest payments on our convertible subordinated notes. If adequate funds are not available, we may be required to curtail significantly or discontinue one or more of our research, drug discovery or development programs, including clinical trials, or attempt to obtain funds through arrangements with collaborative partners or others that may require us to relinquish rights to certain of our technologies or products in research or development. Additional financing may not be available on acceptable terms, if at all.

OUR SALES AND MARKETING EXPERIENCE IS LIMITED.

We currently have little experience in marketing and selling pharmaceutical products. We must either develop a marketing and sales force or enter into arrangements with third parties to market and sell any of our product candidates which are approved by the FDA. We do not know whether we will be able to enter into marketing and sales agreements with others on acceptable terms, if at all. We may bring merimepodib to market ourselves. If so, we may not be able to successfully develop our own sales and marketing force for this drug candidate and our other drug candidates for which we have retained marketing or co-promotion rights. If we develop our own marketing and sales capability, we may be competing with other companies that currently have experienced and well-funded marketing and sales operations. We have granted exclusive marketing rights for Agenerase and VX-175 to GlaxoSmithKline worldwide except the Far East, and for pralnacasan to Aventis worldwide. Kissei has exclusive marketing rights to Agenerase and VX-702 in Japan. Even though we retain some co-promotion rights, to the extent that our collaborative partners have commercial rights to our products, any revenues we receive from those products will depend primarily on the sales and marketing efforts of others.

IF WE INCUR PRODUCT LIABILITY EXPENSES, OUR EARNINGS COULD BE NEGATIVELY IMPACTED.

Our business will expose us to potential product liability risks that arise from the testing, manufacturing and sales of our products. In addition to direct expenditures for damages, settlement and defense costs, there is the possibility of adverse publicity as a result of product liability claims. These risks will increase as our products receive regulatory approval and are commercialized. We currently carry \$15 million (aggregate) of product liability insurance. This level of insurance may not be sufficient. Moreover, we may not be able to maintain our existing levels of insurance or be able to obtain or maintain additional insurance that we may need in the future on acceptable terms.

In addition, our research and development activities may from time to time involve the controlled use of hazardous materials, including hazardous chemicals and radioactive materials. Accordingly, we are subject to federal, state and local laws governing the use, handling and disposal of these materials. Although we believe that our safety procedures for handling and disposing of hazardous materials comply with regulatory requirements, we cannot completely eliminate the risk that accidental contamination or injury from these materials could expose us to significant liability.

WE HAVE ADOPTED ANTI-TAKEOVER PROVISIONS THAT MAY FRUSTRATE ANY ATTEMPT TO REMOVE OR REPLACE OUR CURRENT MANAGEMENT.

Our corporate charter and by-law provisions and stockholder rights plan may discourage certain types of transactions involving an actual or potential change of control of Vertex which might be beneficial to the company or its securityholders. Our charter provides for staggered terms for the members of the Board of Directors. Our by-laws grant the directors a right to adjourn annual meetings of stockholders, and certain provisions of the by-laws may be amended only with an 80% stockholder vote. Pursuant to our stockholder rights plan, each share of common stock has an associated preferred share purchase right. The rights will not trade separately from the common stock until, and are exercisable only upon, the acquisition or the potential acquisition through tender offer by a person or group of 15% or more of the outstanding common stock. We may issue shares of any class or series of preferred stock in the future without stockholder approval and upon such terms as our Board of Directors may determine. The rights of the holders of common stock will be subject to, and may be adversely affected by, the rights of the holders of any class or series of preferred stock that may be issued in the future. As a result, shareholders or other parties may find it more difficult to remove or replace our current management.

OUR STOCK PRICE MAY FLUCTUATE BASED ON FACTORS BEYOND OUR CONTROL.

Market prices for securities of companies such as Vertex are highly volatile. Within the 12 months ended December 31, 2001, our common stock traded between \$75.17 and \$15.50. The market for our stock, like that of other companies in the biotechnology field, has from time to time experienced significant price and volume fluctuations that are unrelated to our operating performance. The future market price of our securities could be significantly and adversely affected by factors such as:

- announcements of results of clinical trials;
- technological innovations or the introduction of new products by our competitors;
- government regulatory action;
- public concern as to the safety of products developed by others;
- developments in patent or other intellectual property rights or announcements relating to these matters;
- developments in domestic and international governmental policy or regulation, for example relating to intellectual property rights; and

- developments and market conditions for pharmaceutical and biotechnology stocks, in general.

OUR OUTSTANDING INDEBTEDNESS MAY INCREASE OUR COSTS AND MAKE IT MORE DIFFICULT TO OBTAIN ADDITIONAL FINANCING.

As of December 31, 2001, we had approximately \$323 million in long-term debt. The high level of our indebtedness will impact us by:

- significantly increasing our interest expense and related debt service costs;
- making it more difficult to obtain additional financing for working capital, capital expenditures, debt service requirements or other purposes; and
- constraining our ability to react quickly in an unfavorable economic climate.

ITEM 2. PROPERTIES

We lease an aggregate of approximately 334,000 square feet of laboratory and office space in seven facilities in Cambridge, Massachusetts. The leases have expiration dates ranging from 2002 to 2010. We have the option to extend the lease for our headquarters facility at 130 Waverly Street, Cambridge, for up to two additional terms, ending in 2015 with respect to one portion of the building, and in 2019 for the other portion of the building. The lease for the laboratory and office building adjacent to our headquarters will expire in 2010 with the option to extend the lease for up to two additional consecutive ten year terms. We have entered into another agreement to lease approximately 275,000 square feet of laboratory and office space presently under construction in Kendall Square, Cambridge, Massachusetts. That lease will expire in 2017, with the option to extend the lease for two consecutive terms of 10 years each.

We also lease approximately 81,200 square feet of laboratory and office space in San Diego, California. The lease for this space will expire on August 31, 2008, with an option to extend for up to two additional terms of 5 years each. We also sublease an additional 12,500 square feet of space for our administrative functions in a nearby facility. The sublease for this additional space will expire on March 31, 2004, subject to a six-month extension of the sublease upon the mutual agreement of the parties. We also sublease an additional 19,670 square feet of laboratory, office and equipment manufacturing space under a sublease that will expire on July 31, 2002, subject to an option to extend an additional three months expiring on October 31, 2002. To meet our expected growth needs in San Diego, we are currently in negotiations for the purchase of a parcel of land adjacent to our current main building on which we plan to construct additional facilities.

We also currently occupy 1,236 square feet of space in Iowa City, Iowa under a lease that expires April 30, 2003. Our Iowa facility houses the operations Aurora acquired from Quorum Sciences in 2000. In addition, we own one building in Madison, Wisconsin housing PanVera's operations, consisting of approximately 52,000 square feet for research and development, manufacturing, marketing and sales administrative functions. The building is on leased land. The term of the lease will expire on December 31, 2048, subject to our option to extend for an additional twenty years.

We lease approximately 22,000 square feet of laboratory and office space in Milton Park, Abingdon, England, under a lease expiring in 2013, with a right of early termination in 2008, for our U.K. business and research and development activities.

We believe our facilities are adequate for our current needs. We believe we can obtain additional space on commercially reasonable terms.

ITEM 3. LEGAL PROCEEDINGS

Chiron Corporation filed suit on July 30, 1998 against Vertex and Eli Lilly in the United States District Court for the Northern District of California, alleging infringement by the defendants of three U.S. patents issued to Chiron. The infringement action relates to research activities by Vertex and Eli

Lilly in the hepatitis C viral protease field and the alleged use of inventions claimed by Chiron in connection with that research. Chiron has requested damages in an unspecified amount, as well as an order permanently enjoining Vertex and Eli Lilly from unlicensed use of the claimed Chiron inventions. During 1999, Chiron requested and was granted a reexamination by the U.S. Patent and Trademark Office of all three of the patents involved in the suit. Chiron also requested and, over the opposition of Vertex and Eli Lilly, was granted a stay in the infringement lawsuit, pending the outcome of the patent reexamination. The reexamination process is still ongoing and the stay is still in effect. However, a Notice of Intent to Issue a Reexamination Certificate has been issued in two of the three Chiron patents in suit. While the length of the stay and the final outcome of the lawsuit cannot be determined, we maintain that Chiron's claims are without merit and intend to defend the lawsuit, if and when it resumes, vigorously.

On December 7, 2001, Oregon Health Sciences University filed suit against Vertex in the District Court of Oregon. The complaint in the suit seeks to name Dr. Bruce Gold, an employee of Oregon Health Sciences University, as an inventor and Oregon Health Sciences University as part owner of five of Vertex's neurophilin patents. The suit stems from assays run on Vertex compounds by Dr. Gold under a sponsored research agreement in 1996. We have investigated the inventorship on these patents and believe that Dr. Gold is not an inventor, Oregon Health Sciences University has no ownership interest in any of these patents, and that the claims made in this complaint are without merit. We intend to contest this claim vigorously.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

There were no matters submitted to a vote of security holders during the fourth quarter of the fiscal year ended December 31, 2001.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

Our common stock trades on the Nasdaq Stock Market (Nasdaq) under the symbol "VRTX." The following table sets forth for the periods indicated the high and low sale prices per share of the common stock as reported by Nasdaq:

<u>Year Ended December 31, 2000:</u>	<u>High</u>	<u>Low</u>
First quarter	\$45.19	\$16.50
Second quarter	58.00	18.88
Third quarter	96.00	46.00
Fourth quarter	99.25	51.50
<u>Year Ended December 31, 2001:</u>		
First quarter	\$75.17	\$25.63
Second quarter	52.25	29.75
Third quarter	49.38	15.50
Fourth quarter	28.84	16.74

The last sale price of the common stock on March 26, 2002, as reported by Nasdaq, was \$27.33 per share. As of March 26, 2002, there were 439 holders of record of the common stock (approximately 23,500 beneficial holders).

We have never declared or paid any cash dividends on our common stock, and we currently expect that future earnings, if any, will be retained for use in our business.

ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA (Unaudited)

The following selected financial data for each of the five years in the period ended December 31, 2001 are derived from our consolidated financial statements. This data should be read in conjunction with our audited consolidated financial statements and related notes, and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	Year Ended December 31,				
	2001(1)	2000(2)	1999	1998	1997
	(In thousands, except per share amounts)				
Consolidated Statement of Operations Data:					
Revenues:					
Royalties	\$ 11,119	\$ 12,361	\$ 8,398	—	—
Product sales	59,921	52,437	44,208	\$ 26,240	\$ 14,735
Services	27,466	20,245	12,911	7,181	5,053
Collaborative and other R&D	68,984	68,239	43,370	29,145	29,926
Total revenue	167,490	153,282	108,887	62,566	49,714
Costs and expenses:					
Royalty payments	3,786	4,134	3,108	—	—
Cost of product sales	25,242	31,127	27,236	24,093	6,979
Cost of service revenues	10,601	8,357	4,237	3,017	2,813
Research and development	148,673	101,093	85,029	76,872	57,792
Sales, general and administrative	47,337	46,014	40,918	26,235	16,242
Merger related costs	23,654	—	—	—	—
Total costs and expenses	259,293	190,725	160,528	130,217	83,826
Loss from operations	(91,803)	(37,443)	(51,641)	(67,651)	(34,112)
Other income, net	23,382	20,239	10,487	16,644	14,770
Debt conversion expense	—	(14,375)	—	—	—
Loss before cumulative effects of changes in accounting principles and extraordinary items	(68,421)	(31,579)	(41,154)	(51,007)	(19,342)
Cumulative effect of change in accounting principle—revenue recognition	(25,901)	(3,161)	—	—	—
Cumulative effect of change in accounting principle—derivatives	17,749	—	—	—	—
Extraordinary gain on early extinguishment of debt	10,340	—	—	—	—
Net loss	\$ (66,233)	\$ (34,740)	\$ (41,154)	\$ (51,007)	\$ (19,342)
Basic and diluted net loss per common share	\$ (0.89)	\$ (0.51)	\$ (0.66)	\$ (0.83)	\$ (0.35)
Basic and diluted weighted average number of common shares outstanding	74,464	67,682	62,602	61,741	55,228
Pro forma amounts assuming the 2001 accounting change relating to revenue recognition is applied retroactively(1)					
Net loss	\$ (40,332)	\$ (45,860)	\$ (38,234)	\$ (56,758)	\$ (23,121)
Net loss per weighted common share — basic and diluted	\$ (0.54)	\$ (0.68)	\$ (0.61)	\$ (0.92)	\$ (0.42)
	December 31,				
	2001	2000	1999	1998	1997
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	\$ 743,202	\$ 814,061	\$ 224,955	\$ 274,638	\$ 329,900
Total assets	925,131	941,136	307,338	321,521	361,704
Obligations under capital lease, loan and notes payable, less current portion	323,026	357,269	16,003	12,484	10,179
Accumulated deficit	(314,532)	(248,299)	(213,164)	(172,009)	(121,002)
Total stockholders' equity	475,351	514,011	251,917	286,056	331,827

(1) During 2001 we implemented a change in accounting principle relating to revenue recognition that was retroactive to January 1, 2001. Please refer to Note C: "Change in Accounting Principle—Revenue Recognition" in the notes to our consolidated financial statements for further information.

(2) In the fourth quarter of 2000, we changed our method of accounting for revenue recognition in conjunction with our adoption of the SEC's Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements" which was retroactive to January 1, 2000. Please refer to Note C: "Change in Accounting Principle—Revenue Recognition" in the notes to our consolidated financial statements for further information.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

We are a global biotechnology company. We seek to discover, develop, and commercialize major pharmaceutical products independently and with collaborators. Chemogenomics, our proprietary, systematic, genomics-based platform, is designed to accelerate the discovery of new drugs and to expand intellectual property coverage of drug candidate compounds and classes of related compounds. We believe this approach, which targets gene families, has formed the basis for successful drug discovery and for the advancement of drug candidates by Vertex and its collaborators. We are developing several drug candidates in commercial collaborations in which we retain rights to downstream product revenue. We have four research facilities worldwide with over 1,000 employees. Our facilities are located in Cambridge, MA, Madison, WI, San Diego, CA and Abingdon, UK.

Our first approved product is Agenerase (amprenavir), an HIV protease inhibitor, which we co-promote with GlaxoSmithKline. We earn a royalty from GlaxoSmithKline on sales of Agenerase. Agenerase has received approval in 34 countries worldwide, including the United States, the 15 member states of the European Union (E.U.), and Japan, where the drug is sold under the trade name Prozei. We have more than twelve drug candidates in development to treat viral diseases, cancer, autoimmune and inflammatory diseases and neurological disorders.

On July 18, 2001, we completed a merger with Aurora Biosciences Corporation (Aurora). The merger unites Aurora's industry-leading cell biology capabilities with Vertex's integrated drug discovery expertise creating a comprehensive, scalable platform for systematically accelerating drug candidate output in target-rich gene families. Aurora specializes in assay development, screening and cell biology capabilities. Aurora generates revenue primarily from product sales and services related to assay development and specialized screening services and systems. We acquired all of Aurora's outstanding common stock in a tax-free, stock for stock transaction, for approximately 14.1 million shares of Vertex common stock; Aurora's outstanding options were converted into options to purchase 2.6 million shares of Vertex common stock. The merger was accounted for as a pooling of interests.

On March 1, 2001, Aurora completed a merger with PanVera Corporation (PanVera). PanVera is a biotechnology company engaged in the development, manufacture and supply of proteins for evaluation of targets and drug screening assays for high-throughput screening. Aurora acquired all of PanVera's outstanding common stock in a tax-free, stock for stock transaction. The merger was accounted for as a pooling of interests. All references to "Aurora" refer to the combined company of Aurora and PanVera.

Aurora will continue to operate as an independent commercial business, although Vertex has incorporated certain of Aurora's existing and emerging drug discovery technologies into its own gene family-based drug discovery platform.

All prior period consolidated financial statements presented have been restated to include the consolidated results of operations, financial position and cash flows of Aurora as though the merger had been in effect on the dates indicated.

We have significant collaborations with large pharmaceutical companies including Aventis, Eli Lilly, GlaxoSmithKline, Novartis, and Serono. With the addition of Aurora, we have other collaborations with large pharmaceutical companies for assay development, screening services and the development of specialized screening platforms. These collaborations and contracts provide us with financial support and other valuable resources for our research programs, development of our clinical drug candidates, and marketing and sales of our products. We believe that we are positioned to commercialize multiple products in the coming years, which we expect will generate increased milestone payments, product revenues and royalty payments.

We consider our collaborations with Novartis and Aventis material to our business. Novartis has agreed to pay us up to approximately \$600 million in pre-commercial payments, comprised of \$15 million paid upon the signing of the agreement in May 2000, up to \$200 million in product research funding over six years and up to approximately \$400 million in further license fees, milestone

payments and cost reimbursements. These amounts are based on the development of eight drug candidates. In addition, Novartis created a \$200 million loan facility to support certain clinical studies, which we may draw down in increments of up to \$25 million for each drug candidate. To date we have not drawn down against the loan facility. The loan is interest free and Novartis will forgive the full amount of any advances if Novartis accepts the drug candidate for development under our agreement. We will receive royalties on any products marketed as a part of the collaboration and under certain conditions will have co-promotion rights in the U.S. and Europe. We retain the rights to any intellectual property resulting from the collaboration.

Aventis has paid us \$20 million for prior research costs associated with pralnacasan (VX-740) and has agreed to pay us \$62 million in milestone payments for successful development by Aventis of pralnacasan in rheumatoid arthritis, the first targeted indication, as well as similar milestone payments for each additional indication. We have granted Aventis an exclusive worldwide license to develop, manufacture and market pralnacasan as well as an exclusive option for other compounds discovered as part of the research collaboration between Vertex and Aventis that ended in 1997.

Aurora has contracts in place that require the delivery of products, licenses and services throughout 2002. These contracts account for over \$70 million of potential 2002 revenue of which approximately \$12 million relates to one specific contract.

We have incurred operating losses since our inception and expect to incur losses for the foreseeable future. We plan to make significant investments in research and development for our other potential products. We expect that losses will fluctuate from year to year and that such fluctuations may be substantial.

Critical Accounting Policies

Our discussion and analysis of our financial condition and results of operations is based upon our consolidated financial statements that have been prepared in accordance with generally accepted accounting principles in the United States of America. The preparation of these financial statements requires us to make certain estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expense during the reported periods. These items are constantly monitored and analyzed by management for changes in facts and circumstances, and material changes in these estimates could occur in the future. Changes in estimates are recorded in the period in which they become known. We base our estimates on historical experience and various other assumptions that we believe to be reasonable under the circumstances. Actual results may differ from our estimates if past experience or other assumptions do not turn out to be substantially accurate.

In December 2001, the SEC requested that all registrants discuss their "critical accounting policies" in management's discussion and analysis of financial condition and results of operations. A critical accounting policy is a policy that is both important to the portrayal of the company's financial conditions and results, and requires management's most difficult, subjective or complex judgments and estimates. While our significant accounting policies are more fully described in Note B to our consolidated financial statements included in this Annual Report, we consider our revenue recognition policy critical and therefore we have separately outlined this policy below.

Our revenue recognition policies are in accordance with the SEC's Staff Accounting Bulletin No. 101 (SAB 101), "Revenue Recognition in Financial Statements". We generate revenue through collaborative research and development agreements, product sales, assay development and screening services and royalty agreements.

Our collaborative and other research and development revenue is primarily generated through collaborative research and development agreements with strategic partners for the development of small molecule drugs that address major unmet medical needs. The terms of the agreements typically

include non-refundable up-front license fees, funding of research and development efforts, payments based upon achievement of certain at-risk and substantive milestones and royalties on product sales.

Under the Substantive Milestone Method, adopted retroactively to January 1, 2001, we recognize revenue from non-refundable, up-front license fees and milestones, not specifically tied to a separate earnings process, ratably over the contracted or estimated period of performance. Changes in estimates could impact revenue in the period the estimate is changed. Research funding is recognized as earned, ratably over the period of effort. Milestones that are based on designated achievement points and that are considered at risk and substantive at the inception of the collaborative contract, are recognized as earned, when the corresponding payment is considered reasonably assured. We evaluate whether milestones are at risk and substantive based on the contingent nature of the milestone, specifically reviewing factors such as the technological and commercial risk that must be overcome and the level of investment required.

Product sales include instrumentation system sales, technology licensing and biotechnology product sales as well as commercial drug substance sales. Revenue from licenses where we have continuing obligations is recognized over the period of the license. Revenue from perpetual licenses is recognized when the license is issued, provided that there are no significant continuing obligations and the payment is non-refundable and non-creditable.

Revenue from sales of commercial drug substance, biotechnology products and certain instrumentation system sales, is recognized upon shipment, when the title to the product and associated risk of loss has passed to the customer, collectibility is reasonably assured and, if applicable, upon acceptance when acceptance criteria are specified or upon expiration of the acceptance period. Sales under long-term production contracts are recognized using percentage of completion accounting, based on actual costs incurred to date compared to total estimated costs to complete. Funding for prototype instrumentation systems was recognized ratably over the terms of the agreements, which approximated costs incurred. Milestones related to delivery of the components of the prototype systems were recognized when earned, as evidenced by written acknowledgement of acceptance from the customer.

Service revenues include assay development, screening services and contracted product development. Service revenue is recognized as the services are performed or ratably over the service period if we believe such method will approximate the expense being incurred. Revenue from upfront fees is deferred and recognized over the service period.

Aurora has certain contracts under which it agrees to sell instrumentation systems and technology licenses in addition to providing assay development and screening services. Each of these separable elements may be individually delivered and is not considered essential to the functionality of the others. We allocate revenue under such contracts to each of the separable elements based on the relative fair value of each element, which under most of our agreements approximates the stated price in the contract.

Royalty revenue is recognized based upon actual and estimated net sales of licensed products in licensed territories, as provided by our collaborative partner, and is generally recognized in the period the sales occur. Differences between actual royalty revenues and estimated royalty revenues, which have not been historically significant, are reconciled and adjusted for in the quarter they become known.

Results of Operations

In the third quarter of 2001, in connection with our overall review of accounting policies concurrent with our merger with Aurora, we elected to change our revenue recognition policy for collaborative and other research and development revenues from the Emerging Issues Task Force No. 91-6 (EITF 91-6) method to the Substantive Milestone Method. We believe this method is preferable because it is reflective of the Company's on-going business operations and is more consistent with the industry practices following the prior year implementation of SAB 101 throughout the biotechnology industry.

In the fourth quarter of 2000, we changed our method of accounting for revenue recognition for collaborative and other research and development revenues to the EITF 91-6 method in conjunction with our adoption of SAB 101. Under the EITF 91-6 method, adopted retroactively to January 1, 2000, we recognized revenue from research and development arrangements, including non-refundable upfront license fees, milestones and research and development funding, over the period of our continuing involvement using the lesser of the non-refundable cash received or the result achieved using percentage of completion accounting. Where we had no continuing involvement, non-refundable license fees were recorded as revenue upon receipt and milestones were recorded as revenue upon achievement of the milestone by the collaborative partner.

The cumulative effect of the 2001 change in accounting principle related to revenue recognition recorded in the third quarter of 2001, retroactive to January 1, 2001, resulted in a non-cash charge to income of \$25,901,000. The cumulative effect of the change in accounting principle relating to the adoption of SAB 101 in the fourth quarter of 2000, retroactive to January 1, 2000, resulted in a non-cash charge to income of \$3,161,000.

The January 1, 2001 charge to income resulted in revenue of \$7,748,000 being recognized in 2001 that was recognized in prior periods. Additionally, \$6,979,000, \$2,809,000, \$2,580,000 and \$5,785,000 will be recognized as revenue in 2002, 2003, 2004 and thereafter, respectively, which was included in the January 2001 charge to income.

The following discussions relating to net loss, net loss per basic and diluted common share and revenue for the years ended December 31, 2000 and 1999 reflect the pro forma results as if we had followed the Substantive Milestone Method of revenue recognition from our inception. Actual results for 2001 reflect the adoption of the Substantive Milestone Method as of January 1, 2001.

Year Ended December 31, 2001 Compared with Year Ended December 31, 2000

Our net loss for 2001 was \$40,332,000 or \$0.54 per basic and diluted common share including merger related expenses of \$23,654,000, compared to a net loss of \$45,860,000 or \$0.68 per basic and diluted share in 2000.

Total revenues increased to \$167,490,000 in 2001 compared to \$139,001,000 in 2000. In 2001, revenue was comprised of: \$11,119,000 in royalty revenue, \$59,921,000 in product sales revenue, \$27,466,000 in service revenue and \$68,984,000 in collaborative and other research and development revenue, as compared with \$12,361,000 in royalty revenue, \$52,437,000 in product sales revenue, \$20,245,000 in service revenue and \$53,958,000 in collaborative and other research and development revenue in 2000.

Royalties consist primarily of Agenerase royalty revenue. Agenerase royalty revenue is based on estimated and actual worldwide net sales of Agenerase.

Product sales include instrumentation sales, technology licensing and biotechnology product sales as well as sales of commercial drug substance.

Product sales increased \$7,484,000, or 14%, to \$59,921,000 in 2001 from \$52,437,000 in 2000. The increase in product sales in 2001 from 2000 is due to increased technology licensing revenue and increased biotechnology product revenue, partially offset by a decrease in instrumentation revenue. Instrumentation revenue decreased in 2001 from 2000 due to the completion and delivery of several significant products and services in late 2000 and early 2001, that have not been replaced, due in part to Aurora's strategic shift in focus toward technology licensing and discovery service activity. The increase in biotechnology revenue is attributed to a continued increase in demand for protein drug targets, drug screening assays and other biotechnology products.

Service revenue includes assay development, screening services and contracted product development.

Service revenue increased to \$27,466,000 in 2001 from \$20,245,000 in 2000. The increase in service revenue is attributable to new strategic alliances and screening collaborations entered into in late 2000 and early 2001.

Collaborative and other research and development revenue consists of research support payments, development reimbursements, milestones and amortization of previously received up-front or license payments.

Collaborative and other research and development revenue increased in 2001 by 28% or \$15,026,000 as compared with 2000 due primarily to collaborative agreements signed in May and December of 2000. In 2001 we recognized \$36,723,000 of revenue under the Novartis collaboration compared with \$14,823,000 in 2000. In an agreement signed in May 2000, we agreed with Novartis to collaborate to discover, develop and commercialize small molecule drugs targeted at the kinase protein family. Effort related to the kinase research program increased significantly in 2001. In December 2000 we entered into a collaboration with Serono to discover, develop and market caspase inhibitors. In connection with the Serono agreement we recognized \$4,802,000 in revenue during 2001 compared with \$397,000 during 2000. In May 2000 we received and recognized as revenue a \$10,000,000 license payment from Aventis under a collaborative agreement covering the development of pralnacasan (VX-740), an orally active inhibitor of interleukin-1 beta converting enzyme (ICE). Aventis has exclusive worldwide license to develop, manufacture and market pralnacasan as well as an exclusive option for other compounds discovered as part of the collaboration that ended in 1997. The balance of collaborative and other research and development revenue for 2001 and 2000 is made up of research support payments, development reimbursements and milestones from other collaborative partners.

Royalty costs of \$3,786,000 and \$4,134,000 in 2001 and 2000, respectively, consist primarily of royalty payments on the sales of Agenerase.

Product costs decreased \$5,885,000 or 19% to \$25,242,000 in 2001 from \$31,127,000 in 2000. The decrease in product costs is attributable to a strategic shift in focus of the Aurora business towards technology licensing and discovery services activity. Instrumentation revenue, which has lower gross margins, decreased during the year, while technology license and biotechnology product revenue, which has higher gross margins, increased during the year.

Cost of service revenue increased from \$8,357,000 in 2000 to \$10,601,000 in 2001, primarily due to a related increase in service revenue.

Research and development expenses increased to \$148,673,000 in 2001 from \$101,093,000 in 2000 primarily due to the continued expansion of our research and development operations, an increase in the number of drug development candidates from eight candidates at December 31, 2000 to more than twelve candidates at December 31, 2001 and the continued shift of Aurora's strategy towards drug discovery activity. During 2001 there was a significant increase in research and discovery activities associated with our gene family programs, specifically our kinase research program being conducted under our Novartis collaboration, and our protease research program. Development expenses increased as we continued to advance our drug candidates with substantial investment in our p38 MAP kinase (specifically VX-745) and our IMPDH programs. Also, related to our expansion were increases in personnel, facilities expenses and equipment depreciation.

We have more than 12 drug candidates in development targeting a range of major diseases. Our collaborative partners have agreed to fund portions of our research and development programs and/or

to conduct certain research and development related to specified drug candidates. Collaborator and Company-sponsored research and development expenses for 2001 and 2000 were as follows:

	2001			2000		
	Research	Development	Total	Research	Development	Total
	<i>(In thousands)</i>					
Collaborator-Sponsored	\$49,490	\$20,262	\$ 69,752	\$43,253	\$ 8,757	\$ 52,010
Company-Sponsored	50,112	28,809	78,921	30,508	18,575	49,083
Total	<u>\$99,602</u>	<u>\$49,071</u>	<u>\$148,673</u>	<u>\$73,761</u>	<u>\$27,332</u>	<u>\$101,093</u>

To date we have incurred in excess of \$630,000,000 in research and development costs associated with drug discovery and development. As of December 31, 2001 we had 570 full-time employees dedicated to research and development across our four research facilities. We anticipate research and development expenses will continue to increase as we add personnel and expand research and development activities to accommodate our existing collaborations and additional commitments we may undertake in the future.

We estimate that it takes 10 to 15 years (industry average is 12 years) to discover, develop and bring to market a pharmaceutical product. Drug development in the U.S. is a process that includes several steps defined by the FDA as outlined below:

Phase:	Objective:	Estimated Duration:
Discovery	Lead identification and target validation	2 to 4 years
Pre-Clinical	Toxicology to identify risks for humans; gather early pharmacokinetic data	1 to 2 years
Phase I	Establish safety in humans, study how the drug works, metabolizes and interacts with other drugs	1 to 2 years
Phase II	Establish effectiveness of the drug and its optimal dosage	2 to 4 years
Phase III	Confirm efficacy, dosage regime and safety profile of the drug	2 to 4 years
FDA approval	Approval by the FDA to sell and market the drug under certain prescribed labelling	6 mths to 2 years

The successful development of our products is highly uncertain and subject to a number of risk factors. The duration of clinical trials may vary substantially according to the type, complexity and novelty of the pharmaceutical product. The FDA and comparable agencies in foreign countries impose substantial requirements on the introduction of therapeutic pharmaceutical products through lengthy and detailed laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures. Data obtained from pre-clinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The duration and the cost related to discovery, pre-clinical and clinical trials may vary significantly over the life of a project and are difficult to predict. The most significant costs associated with drug discovery and development are those costs associated with Phase II and Phase III clinical trials.

Below is a summary of our drug candidates currently in clinical development:

Drug	Clinical Indications	Phase	Program	Collaborator
INFECTIOUS DISEASE				
VX-175	HIV	III	HIV	GlaxoSmithKline
Merimepodib (VX-497)	Chronic hepatitis C	II	IMPDH	—
VX-950	Chronic hepatitis C	Preclin	Hepatitis C protease	Eli Lilly
VX-799	Sepsis	Preclin	Caspases	Serono; Taisho
VX-385	HIV	Preclin	HIV	GlaxoSmithKline
INFLAMMATION AND AUTOIMMUNE DISEASE				
Pralnacasan (VX-740)	Rheumatoid arthritis (RA); inflammatory diseases	II	ICE	Aventis
VX-148	Psoriasis; autoimmune diseases	I	IMPDH	—
VX-944	Autoimmune diseases	Preclin	IMPDH	—
VX-850	Inflammatory diseases	Preclin	p38 MAP Kinase	Kissei
VX-702	Inflammatory diseases	Preclin	p38 MAP Kinase	Kissei
VX-765	Inflammatory diseases	Preclin	ICE	—
CANCER				
Incel™	Multidrug resistant solid tumor cancers	II	MDR	—
VX-853	Multidrug resistant solid tumor cancers	I/II	MDR	—
GENETIC DISORDERS				
VX-563	Multiple indications	Preclin	Histone Deacetylase	—

Sales, general and administrative expenses remained relatively consistent totaling \$47,337,000 in 2001 compared with \$46,014,000 in 2000. We expect sales, general and administrative expenses to remain consistent with current levels over the next year.

Merger related costs of \$23,654,000 consisted of investment banking, legal and accounting fees associated with the acquisition of Aurora completed on July 18, 2001.

Interest income increased approximately \$11,821,000 to \$45,133,000 in 2001 from \$33,312,000 in 2000. The increase is due to a higher level of cash and marketable securities for the full year of 2001 compared with 2000. The increase in cash and marketable securities is primarily a result of the proceeds received from the issuance in September 2000 of \$345,000,000 of 5% convertible subordinated notes due September 2007 (September Notes). In March 2000 we issued \$175,000,000 of convertible subordinated notes (March Notes), which we called for redemption in September 2000 and which were subsequently converted to equity.

Interest expense increased to approximately \$19,318,000 in 2001 from \$11,653,000 in 2000. The increase is due to interest expense associated with the September Notes.

Using the equity method of accounting we recorded \$662,000 as our share of loss in Altus Biologics Inc. (Altus), for the year ended December 31, 2001, compared with \$550,000 as our share of loss for the year ended December 31, 2000. The loss is included in other, net on the Statement of

Operations. Effective September 28, 2001, coincident with a financial restructuring of Altus, we changed our method of accounting for Altus from the equity method to the cost method. Please see Note H to our consolidated financial statements included in this report.

Effective July 1, 2001, we adopted Derivative Implementation Group Issue No. A17, "Contracts that Provide for Net Share Settlement" (DIG A17). Pursuant to the adoption of DIG A17 we recorded a \$17,749,000 cumulative effect of a change in accounting principle to reflect the value of warrants held in Altus. This amount is included in investments in the December 31, 2001 balance sheet. As of September 30, 2001, the warrants no longer qualified as derivatives under DIG A17 due to changes in the terms of the warrants coincident with a financial restructuring of Altus.

In October 2001, we re-purchased \$30,000,000 in principal amount of our September Notes for cash consideration of \$18,900,000. As a result of this transaction we recorded an extraordinary gain on the early extinguishment of debt of \$10,340,000, net of \$760,000 of deferred debt costs in the fourth quarter of 2001.

Year Ended December 31, 2000 Compared with Year Ended December 31, 1999

Our net loss for 2000 was \$45,860,000, or \$0.68 per basic and diluted share, compared to a net loss of \$38,234,000 or \$0.61 per basic and diluted share in 1999.

Total revenues increased to \$139,001,000 in 2000 from \$111,807,000 in 1999. In 2000 revenue was comprised of \$12,361,000 in royalty revenue, \$52,437,000 in product sales, \$20,245,000 in service revenues, and \$53,958,000 in collaborative and other research and development revenue, compared with \$8,398,000 in royalty revenue, \$44,208,000 in product sales, \$12,911,000 in service revenues and \$46,290,000 in collaborative and other research and development revenue in 1999.

Product sales increased \$8,229,000, or 19%, from \$44,208,000 in 1999 to \$52,437,000 in 2000. The increase in product sales is due primarily to increases in licensing revenue and biotechnology product revenue. The increase in licensing revenue is attributable to several significant license agreements executed in mid to late 2000. The increase in biotechnology product revenue can be attributed to increased demand for protein drug targets and drug screening assays.

Service revenue increased significantly during the year 2000, from \$12,911,000 in 1999 to \$20,245,000 in 2000. The increase in service revenue is attributable to several significant service agreements entered into in late 1999 and early 2000.

In 2000 we recognized \$53,958,000 in collaborative and other research and development revenue. Approximately \$14,823,000 of our collaborative and other research and development revenue earned in 2000 was earned under the Novartis collaboration. Additionally we received and recognized as revenue a \$10,000,000 license payment from Aventis under our collaborative agreement and a \$3,000,000 substantive milestone payment for the approval of Agenerase in the E.U. The balance of our collaborative and other research and development revenue in 2000 was earned under other collaborations consisting of research support payments, development reimbursements and amortization of previously received up-front or license payments. Comparatively, in 1999 we recognized \$46,290,000 in collaborative and other research and development revenue. This included a \$10,000,000 initial license payment and a \$5,000,000 substantive milestone payment in connection with the signing of the Aventis agreement as well as a \$5,000,000 substantive milestone payment for the U.S. FDA approval of Agenerase. The balance of collaborative and other research and development revenue recognized during 1999 was earned under other collaborations.

Product costs increased \$3,890,000 or 14% to \$31,127,000 in 2000 from \$27,237,000 in 1999. The increase in product costs resulted from increased purchases of materials and technology development expenses associated with instrumentation revenue and increased expenses associated with biotechnology product revenue. Instrumentation expenses increased at a rate significantly greater than the corresponding revenue due to unanticipated additional resources required to complete certain projects.

Cost of service revenue increased from \$4,236,000 in 1999 to \$8,357,000 in 2000. This was consistent with the increase in service revenue for the same period.

Royalty costs of \$4,134,000 and \$3,108,000 in 2000 and 1999, respectively, primarily consisted of royalty payments on the sales of Agenerase.

Research and development expenses increased to \$101,093,000 in 2000 from \$85,029,000 in 1999. The increase in research and development expenses was principally due to the continued expansion of our research and development operations and an increase in the number of drug development candidates over the prior year. Related to our expansion were increases in personnel, facilities expenses, equipment depreciation and increased technology license payments for access to gene database information. The expenses associated with the expansion were partially offset by a decrease in external development activities associated with certain development candidates.

Sales, general and administrative expenses increased \$5,096,000 during the year 2000, from \$40,918,000 in 1999 to \$46,014,000 in 2000. The increase was primarily a result of increased personnel and professional expenses associated with our growth. Additionally, during 2000 marketing expenses associated with Agenerase increased.

Interest income increased from \$12,954,000 in 1999 to \$33,312,000 in 2000. The increase is due to a higher level of cash and marketable securities throughout 2000 primarily as a result of the proceeds received from the issuance of \$520,000,000 in principal amount of the March Notes and the September Notes. Partially offsetting the increase in interest income was a \$1,400,000 net write down of a marketable security due to management's assessment that the decline in value was other-than-temporary.

Interest expense increased significantly from \$1,704,000 in 1999 to \$11,653,000 in 2000. The increase is due to interest expense associated with the March Notes and the September Notes.

In the third quarter of 2000 we recognized debt conversion expense of \$14,375,000, representing the "make-whole" payment resulting from our call for redemption on September 15, 2000 of our March Notes. As a result of the call for redemption, the holders of the Notes were entitled to a "make-whole" payment of \$82.14 per \$1,000 principal amount of the notes, which was paid in cash on October 5, 2000.

Using the equity method of accounting we recorded \$550,000 as our share of loss in Altus in 2000, compared with \$724,000 as our share of loss in 1999. The loss is included in other, net on the Statement of Operations. Please see Note H to our consolidated financial statements included in this report.

Liquidity and Capital Resources

Our operations have been funded principally through strategic collaborative agreements, strategic technology alliances, revenues from assay development and screening services, product sales, royalties, public offerings and private placements of our equity and debt securities, equipment lease financing, and investment income. With the approval and launch of Agenerase in April 1999, we began receiving product royalty revenues. In 2000, we completed private placements of the March Notes and the September Notes.

We have continued to increase and advance products in our research and development pipeline. Consequently, we expect to incur losses on a quarterly and annual basis as we continue to develop existing and future compounds and to conduct clinical trials of potential drugs. We also expect to incur substantial administrative and commercialization expenditures in the future and additional expenses related to filing, prosecution, defense and enforcement of patent and other intellectual property rights.

We expect to finance these substantial cash needs with future payments under our existing and future collaborative agreements, strategic technology alliances, royalties from the sales of Agenerase, revenues from assay development and screening services, product sales, royalties, existing cash and

marketable securities of \$743,202,000 at December 31, 2001, together with investment income earned thereon, and facilities and equipment financing. To the extent that funds from these sources are not sufficient to fund our activities, it will be necessary to raise additional funds through public offerings or private placements of securities or other methods of financing. There can be no assurance that such financing will be available on acceptable terms, if at all.

Our aggregate cash and marketable securities decreased \$70,859,000 to \$743,202,000, including cash and cash equivalents of \$189,205,000, at December 31, 2001 from \$814,061,000, including cash and cash equivalents of \$346,659,000, at December 31, 2000. Net cash used in operations was \$8,074,000 for the year ended December 31, 2001, which resulted from the net loss of \$66,233,000, offset by \$17,069,000 of net non-cash charges and gains, an increase in deferred revenue of \$20,469,000 and \$20,621,000 of changes in operating assets and liabilities. Deferred revenue increased due to cash received for research funding and receipt of a milestone payment, the majority of which was not recognized as revenue in 2001. Net cash used in investing activities for 2001 was \$145,087,000, which included property and equipment expenditures of \$53,899,000 and net purchases of marketable securities of \$76,595,000. Cash used in financing activities during 2001 was \$3,982,000 including approximately \$18,900,000 for the retirement of \$30,000,000 of principal on our September Notes as well as \$4,735,000 used for the repayment of capital lease and loan obligations. The issuance of common stock under employee stock option and benefit plans for the year ended December 31, 2001 provided \$19,653,000.

Commitments

At December 31, 2001, our future minimum commitments included facilities and certain equipment under non-cancelable operating leases, as well as contractual commitments related to our research and development programs. In January 2001 we entered into an agreement to lease approximately 275,000 square feet of laboratory and office space presently under construction. We will begin paying rent in March 2003. The lease will expire in 2017 with the option to extend the lease for two consecutive terms of ten years each ultimately expiring in 2037. Our commitments under this lease, as well as additional non-cancelable operating leases and contractual, research and development program commitments, are included in the table below (in thousands):

<u>Year</u>	<u>Operating Leases Commitments</u>	<u>R&D Contractual Commitments</u>
2002	\$ 18,706	\$ 6,859
2003	33,481	3,924
2004	32,916	2,209
2005	32,804	865
2006	28,902	—
Thereafter	<u>255,796</u>	<u>—</u>
Total minimum commitments	<u>\$402,605</u>	<u>\$13,857</u>

Forward-looking Statements

This report contains forward-looking statements about our business, including our expectation that (i) we are positioned to commercialize multiple products in the coming years that we expect will generate increased revenues (ii) our losses will continue, (iii) our research and development expenses, our administrative and commercialization expenses and our expenses related to filing, prosecuting and defending our patents and intellectual property rights will increase, and sales, general and administrative expenses will remain consistent with current levels, and (iv) the Chiron Corporation and Oregon Health Sciences University litigation will not have a material adverse effect on us. While management makes its best efforts to be accurate in making forward-looking statements, such statements are subject to risks and uncertainties that could cause our actual results to vary materially. These risks and uncertainties include, among other things, our inability to successfully integrate Aurora

into our existing business, our inability to further identify, develop and achieve commercial success for new products and technologies, the possibility of delays in the research and development necessary to select drug development candidates and delays in clinical trials, the risk that clinical trials may not result in marketable products, the risk that we may be unable to successfully finance and secure regulatory approval of and market our drug candidates, our dependence upon pharmaceutical and biotechnology collaborations, the levels and timing of payments under our collaborative agreements, uncertainties about our ability to obtain new corporate collaborations and acquire new technologies on satisfactory terms, if at all, the development of competing systems, our ability to protect our proprietary technologies, patent-infringement claims, risks of new, changing and competitive technologies and regulations in the U.S. and internationally. Please see the "Risk Factors" appearing elsewhere in this report for more details regarding these and other risks. We disclaim any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

Legal Proceedings

Chiron Corporation (Chiron) filed suit on July 30, 1998 against Vertex and Eli Lilly and Company in the United States District Court for the Northern District of California, alleging infringement by the defendants of three U.S. patents issued to Chiron. The infringement action relates to research activities by Vertex and Eli Lilly in the hepatitis C viral protease field and the alleged use of inventions claimed by Chiron in connection with that research. Chiron has requested damages in an unspecified amount, as well as an order permanently enjoining the defendants from unlicensed use of the claimed Chiron inventions. During 1999, Chiron requested and was granted a reexamination by the U.S. Patent and Trademark Office of all three of the patents involved in the suit. Chiron also requested and, over the opposition of Vertex and Eli Lilly, was granted a stay in the infringement lawsuit, pending the outcome of the patent reexamination. That reexamination proceeding is still on going and the stay is still in effect. However, a Notice of Intent to Issue a Reexamination Certificate has been issued in two of the three Chiron patents in suit. While the length of the stay and the final outcome of the lawsuit cannot be determined, we maintain that Chiron's claims are without merit and intend to defend the lawsuit, if and when it resumes, vigorously.

On December 7, 2001 Oregon Health Sciences University filed suit against Vertex in the District Court of Oregon. The complaint in the suit seeks to name Bruce Gold, an employee of Oregon Health Sciences University, as an inventor and Oregon Health Sciences University as part owner, of five of Vertex's neurophilin patents. The suit stems from assays run on Vertex compounds by Dr. Gold under a sponsored research agreement in 1996. We have investigated the inventorship on these patents and have concluded that Bruce Gold is not an inventor, Oregon Health Sciences University has no ownership interest in any of these patents, and that the claims made in this complaint are without merit. We intend to contest this claim vigorously.

Recent Accounting Pronouncements

In June 2001, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standard ("SFAS") No. 141, "Business Combinations." SFAS No. 141 requires that all business combinations be accounted for under the purchase method only and that certain acquired intangible assets in a business combination be recognized as assets apart from goodwill. SFAS No. 141 is effective for all business combinations initiated after June 30, 2001 and for all business combinations accounted for by the purchase method for which the date of acquisition is after June 30, 2001.

In June 2001, the FASB issued SFAS No. 142, "Goodwill and Other Intangible Assets," which requires that ratable amortization of goodwill be replaced with periodic tests of the goodwill's impairment and that intangible assets other than goodwill be amortized over their useful lives. The provisions of SFAS No. 142 will be effective for fiscal years beginning after December 15, 2001, and will thus be adopted by the Company, as required, on January 1, 2002. We do not expect SFAS No. 142 will have a material effect on our financial position and results of operations.

In October 2001, the FASB issued SFAS No. 144, "Accounting for the Impairment of Long-Lived Assets." SFAS No. 144 supercedes SFAS No. 121, "Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of" and provides a single accounting model for long-lived assets to be disposed of. The provisions of SFAS No. 144 will be effective for fiscal years beginning after December 15, 2001. We do not expect SFAS No. 144 will have on our financial position and results of operations.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As part of its investment portfolio, Vertex owns financial instruments that are sensitive to market risks. The investment portfolio is used to preserve Vertex's capital until it is required to fund operations, including Vertex's research and development activities. None of these market risk sensitive instruments are held for trading purposes. Vertex does not have derivative financial instruments in its investment portfolio.

Interest Rate Risk

Vertex invests its cash in a variety of financial instruments, principally securities issued by the U.S. government and its agencies, investment grade corporate bonds and notes and money market instruments. These investments are denominated in U.S. dollars. All of its interest-bearing securities are subject to interest rate risk, and could decline in value if interest rates fluctuate. Substantially all of Vertex's investment portfolio consists of marketable securities with active secondary or resale markets to help ensure portfolio liquidity, and Vertex has implemented guidelines limiting the term to maturity of its investment instruments. Due to the conservative nature of these instruments, Vertex does not believe that it has a material exposure to interest rate risk.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this Item 8 is contained on pages F-1 through F-38 of this Report.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The information regarding directors required by this Item 10 is included in the definitive Proxy Statement for Vertex's 2002 Annual Meeting of Stockholders, to be filed with the Commission on or about April 9, 2002 (the "2002 Proxy Statement"), under "Election of Directors" and is incorporated herein by reference. The information regarding executive officers required by this Item is included in Part I of this Annual Report on Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item 11 is included in the 2002 Proxy Statement under "Executive Compensation" and is incorporated herein by reference (excluding, however, the "Report on Executive Compensation" and the Performance Graph contained in the 2002 Proxy Statement, which shall not be deemed incorporated herein).

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The information required by this Item 12 is included in the 2002 Proxy Statement under "Security Ownership of Certain Beneficial Owners and Management" and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The information required by this Item 13 is included in the 2002 Proxy Statement under "Employment Contracts and Change in Control Arrangements" and is incorporated herein by reference.

PART IV

ITEM 14. EXHIBITS, FINANCIAL STATEMENT SCHEDULES, AND REPORTS ON FORM 8-K

(a)(1) **Financial Statements.** The Financial Statements required to be filed by Item 8 of this Annual Report on Form 10-K, and filed herewith, are as follows:

	<u>Page Number in this Form 10-K</u>
Reports of Independent Accountants	F-2 to F-4
Consolidated Balance Sheets as of December 31, 2001 and 2000	F-5
Consolidated Statements of Operations for the years ended December 31, 2001, 2000 and 1999	F-6
Consolidated Statements of Stockholders' Equity and Comprehensive Loss for the years ended December 31, 2001, 2000 and 1999	F-7
Consolidated Statements of Cash Flows for the years ended December 31, 2001, 2000 and 1999	F-8
Notes to Consolidated Financial Statements	F-9 to F-38

(a)(2) **Financial Statement Schedules.** Financial Statement Schedules have been omitted because they are either not applicable or the required information is included in the consolidated financial statements or notes thereto.

(a)(3) Exhibits.

Exhibit Number	Exhibit Description
2	Agreement and Plan of Merger dated as of April 29, 2001, by and among Vertex, Aurora and Ahab Acquisition Sub Inc. (filed as Exhibit 2 to Vertex's Current Report on Form 8-K dated April 29, 2001 [File No. 000-19319] and incorporated herein by reference).
3.1	Restated Articles of Organization filed with the Commonwealth of Massachusetts on July 31, 1991 (filed as Exhibit 3.1 to Vertex's 1997 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
3.2	Articles of Amendment filed with the Commonwealth of Massachusetts on June 4, 1997 (filed as Exhibit 3.2 to Vertex's 1997 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
3.3	Certificate of Vote of Directors Establishing a Series of a Class of Stock, as filed with the Secretary of the Commonwealth of Massachusetts on July 31, 1991 (filed as Exhibit 3.3 to Vertex's 1997 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
3.4	By-laws of Vertex as amended and restated as of March 12, 2001 (filed as Exhibit 3.4 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
4.1	Specimen stock certificate (filed as Exhibit 4.1 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).
4.2	Stockholder Rights Plan (filed as Exhibit 4.2 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).
4.3	First Amendment to Rights Agreement dated as of February 21, 1997 (filed as Exhibit 4.3 to Vertex's 1996 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
4.4	Indenture dated as of September 19, 2000 between Vertex and State Street Bank and Trust Company (filed as Exhibit 4.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2000 [File No. 000-19319] and incorporated herein by reference).
4.5	Supplemental Indenture dated as of December 12, 2000 between Vertex and State Street Bank and Trust Company (filed as Exhibit 4.2 to Pre-Effective Amendment No. 1 to the Form S-3 filed by Vertex [Registration No. 333-49844] and incorporated herein by reference).
4.6	Registration Rights Agreement dated as of September 19, 2000 among Vertex and Merrill Lynch & Co., Merrill Lynch, Pierce, Fenner & Smith Incorporated, Credit Suisse First Boston Corporation, Robertson Stephens, Inc., Chase Securities Inc. and J.P. Morgan Securities Inc., as Initial Purchasers (filed as Exhibit 4.2 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2000 [File No. 000-19319] and incorporated herein by reference).
4.7	Second Amendment to Rights Agreement dated as of June 30, 2001 (filed as Exhibit 4.4 to Vertex's Quarterly Report on Form 10-Q for the quarter ended June 30, 2001 [File No. 000-19319] and incorporated herein by reference).
10.1	1991 Stock Option Plan, as amended and restated as of September 14, 1999 (filed as Exhibit 10.1 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.2	1994 Stock and Option Plan, as amended and restated as of September 14, 1999 (filed as Exhibit 10.1 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.3	1996 Stock and Option Plan, Amended and Restated as of March 12, 2001 (filed as

- Exhibit 10.3 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
- 10.4 Non-Competition and Stock Repurchase Agreement between Vertex and Joshua Boger, dated April 20, 1989 (filed as Exhibit 10.2 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).*
- 10.5 Form of Employee Stock Purchase Agreement (filed as Exhibit 10.3 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).*
- 10.6 Form of Employee Non-Disclosure and Inventions Agreement (filed as Exhibit 10.4 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).
- 10.7 Form of Executive Employment Agreement executed by Joshua S. Boger and Vicki L. Sato (filed as Exhibit 10.6 to Vertex's 1994 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
- 10.8 Form of Amendment to Employment Agreement executed by Joshua S. Boger and Vicki L. Sato (filed as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended June 30, 1995 [File No. 000-19319] and incorporated herein by reference).*
- 10.9 Executive Employment Agreement between Vertex and Iain P.M. Buchanan (filed as Exhibit 10.9 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
- 10.10 Agreement dated December 21, 2000 between Vertex and Richard H. Aldrich (filed as Exhibit 10.10 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
- 10.11 Lease dated March 3, 1995, between Fort Washington Realty Trust and Vertex, relating to the premises at 130 Waverly Street, Cambridge, MA (filed as Exhibit 10.15 to Vertex's 1994 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
- 10.12 First Amendment to Lease dated March 3, 1995 between Fort Washington Realty Trust and Vertex (filed as Exhibit 10.15 to Vertex's 1995 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
- 10.13 Second Amendment to Lease and Option Agreement dated June 12, 1997 between Fort Washington Realty Trust and Vertex (filed as Exhibit 10.17 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
- 10.14 Third, Fourth and Fifth Amendments to Lease between Fort Washington Realty Trust and Vertex (with certain confidential information deleted) (filed as Exhibit 10.14 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
- 10.15 Lease by and between Trustees of Fort Washington Realty Trust, Landlord, and Vertex, executed September 17, 1999 (filed as Exhibit 10.27 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1999, with certain confidential information deleted [File No. 000-19319], and incorporated herein by reference).
- 10.16 Lease by and between Kendall Square, LLC, Landlord, and Vertex, executed January 18, 2001 (with certain confidential information deleted) (filed as Exhibit 10.16 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
- 10.17 Agreement for Lease of Premises at 88 Milton Park, Abingdon, Oxfordshire between Milton Park Limited and Vertex Pharmaceuticals (Europe) Limited and Vertex Pharmaceuticals Incorporated (filed as Exhibit 10.18 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).

Exhibit
Number

Exhibit Description

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- 10.18 Research and Development Agreement dated April 13, 1993 between Vertex and Kissei Pharmaceutical Co., Ltd. (with certain confidential information deleted) (filed as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended March 31, 1993 [File No. 000-19319] and incorporated herein by reference).
- 10.19 Research Agreement and License Agreement, both dated December 16, 1993, between Vertex and Burroughs Wellcome Co. (with certain confidential information deleted) (filed as Exhibit 10.16 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1993 [File No. 000-19319] and incorporated herein by reference).
- 10.20 Research and Development Agreement between Vertex and Eli Lilly and Company effective June 11, 1997 (filed with certain confidential information deleted as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended June 30, 1997 [File No. 000-19319] and incorporated herein by reference).
- 10.21 Research and Development Agreement between Vertex and Kissei Pharmaceutical Co. Ltd. effective September 10, 1997 (filed, with certain confidential information deleted, as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1997 [File No. 000-19319] and incorporated herein by reference).
- 10.22 Research Agreement between Vertex and Schering AG dated as of August 24, 1998 (filed, with certain confidential information deleted, as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1998 [File No. 000-19319] and incorporated herein by reference).
- 10.23 License, Development and Commercialization Agreement between Vertex and Hoechst Marion Roussel Deutschland GmbH dated September 1, 1999 (filed with certain confidential information deleted as Exhibit 10.27 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1999 [File No. 000-19319], and incorporated herein by reference).
- 10.24 Collaboration and Option Agreement between Vertex and Taisho Pharmaceutical Co., Ltd. dated November 30, 1999 (filed, with certain confidential information deleted, as Exhibit 10.27 to Vertex's 1999 Form 10-K [File No. 000-19319] and incorporated herein by reference).
- 10.25 Research and Early Development Agreement between Vertex and Novartis Pharma AG dated May 8, 2000 (filed, with certain confidential information deleted, as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended March 31, 2000 [File No. 000-19319] and incorporated herein by reference).
- 10.26 Research Agreement between Vertex and Laboratoires Serono S.A. dated December 11, 2000 (with certain confidential information deleted) (filed as Exhibit 10.26 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
- 10.27 Letter Agreement between Aurora and Stuart J. Collinson (filed as Exhibit 10.26 to Vertex's registration statement on Form S-4 [Registration No. 333-61480] and incorporated herein by reference).*
- 10.28 Executive Employment Agreement between Vertex and Kenneth S. Boger (filed herewith).*
- 10.29 Executive Employment Agreement between Vertex and Ian F. Smith (filed herewith).*
- 10.30 Letter Agreement between Vertex and N. Anthony Coles, M.D. (filed herewith).*
- 18.1 Letter from PricewaterhouseCoopers LLP dated November 14, 2001 re: Change in Accounting Principle (filed as Exhibit 18.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2001 [File No. 000-19319] and incorporated herein by reference).
- 21 Subsidiaries of Vertex (filed herewith).
- 23.1 Consent of Independent Accountants, PricewaterhouseCoopers LLP (filed herewith).

Exhibit
Number

Exhibit Description

- 23.2 Consent of Ernst & Young LLP, Independent Auditors (filed herewith).
23.3 Consent of Independent Public Accountants, Arthur Andersen LLP (filed herewith).

* Compensatory plan or agreement applicable to management and employees.

(b) Reports on Form 8-K. No reports on Form 8-K were filed by Vertex during the quarter ended December 31, 2001.

VERTEX PHARMACEUTICALS INCORPORATED

Index to Consolidated Financial Statements

	<u>Page Number</u>
Reports of Independent Accountants	F-2 to F-4
Consolidated Balance Sheets as of December 31, 2001 and 2000	F-5
Consolidated Statements of Operations for the years ended December 31, 2001, 2000 and 1999	F-6
Consolidated Statements of Stockholders' Equity and Comprehensive Loss for the years ended December 31, 2001, 2000 and 1999	F-7
Consolidated Statements of Cash Flows for the years ended December 31, 2001, 2000 and 1999	F-8
Notes to Consolidated Financial Statements	F-9 to F-38

Report of Independent Accountants

To the Board of Directors and Stockholders of
Vertex Pharmaceuticals Incorporated:

In our opinion, based on our audits and the report of other auditors, the accompanying consolidated balance sheets and the related consolidated statements of operations, of stockholders' equity and comprehensive loss and of cash flows present fairly, in all material respects, the financial position of Vertex Pharmaceuticals Incorporated and its subsidiaries at December 31, 2001 and 2000, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2001 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management; our responsibility is to express an opinion on these financial statements based on our audits. The consolidated financial statements give retroactive effect to the merger of Aurora Biosciences Corporation (formed on March 1, 2001 as a result of the consolidation of Aurora Biosciences Corporation and PanVera Corporation) on July 18, 2001 in a transaction accounted for as a pooling of interests, as described in Note B to the consolidated financial statements. We did not audit the financial statements of Aurora Biosciences Corporation at December 31, 2000 and for each of the years ended December 31, 2000 and 1999, which statements reflect total assets of 18 percent of the related consolidated totals as of December 31, 2000 and total revenues of 49 percent and 54 percent of the related consolidated totals for the years ended December 31, 2000 and 1999, respectively. Those statements were audited by other auditors whose report thereon has been furnished to us, and our opinion expressed herein, insofar as it relates to the amounts included for Aurora Biosciences Corporation, is based solely on the report of the other auditors. We conducted our audits of these statements in accordance with auditing standards generally accepted in the United States of America, which require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits and the report of other auditors provide a reasonable basis for our opinion.

As discussed in Note C to the consolidated financial statements, during each of the years ended December 31, 2001 and 2000 the Company changed its method of accounting for revenue recognition. As discussed in Note H to the consolidated financial statements, during the year ended December 31, 2001 the Company changed its method of accounting for certain derivatives.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
February 5, 2002

Report of Ernst & Young LLP, Independent Auditors

To the Board of Directors and Stockholders
Aurora Biosciences Corporation:

We have audited the accompanying consolidated balance sheet of Aurora Biosciences Corporation (formed as a result of the consolidation of Aurora Biosciences Corporation and PanVera Corporation) as of December 31, 2000 and the related consolidated statements of operations, stockholders' equity, and cash flows for the years ended December 31, 2000 and 1999 (not included separately herein). The consolidated financial statements give retroactive effect to the merger of Aurora Biosciences Corporation and PanVera Corporation on March 1, 2001, which has been accounted for using the pooling of interests method as described in the notes to the consolidated financial statements; such notes also describe the process of consolidation, given that PanVera Corporation's fiscal years were September 30. These consolidated financial statements are the responsibility of the Companies' management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We did not audit the statement of operations of PanVera Corporation for the years ended September 30, 2000 and 1999, which reflect revenues constituting approximately 14.4% of the related combined total for the two-year period ended December 31, 2000. Those statements were audited by other auditors whose reports have been furnished to us, and our opinion, insofar as it relates to data included for PanVera Corporation for the periods described above is based solely on the report of the other auditors.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits and the reports of other auditors provide a reasonable basis for our opinion.

In our opinion, based on our audits and the reports of other auditors, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Aurora Biosciences Corporation at December 31, 2000, and the consolidated results of its operations and its cash flows for the years ended December 31, 2000 and 1999, after giving retroactive effect to the merger of PanVera Corporation, as described in the notes to the consolidated financial statements, in conformity with accounting principles generally accepted in the United States.

/s/ ERNST & YOUNG LLP

San Diego, California
April 27, 2001

Report of Independent Public Accountants

To the Board of Directors and Shareholders of
PanVera Corporation:

We have audited the accompanying balance sheets of PanVera Corporation (a Wisconsin corporation) as of September 30, 2000 and 1999, and the related statements of income, stockholders' equity, and cash flows for the years then ended (not included separately herein). These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of PanVera Corporation as of September 30, 2000 and 1999, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States.

/s/ ARTHUR ANDERSEN LLP

Milwaukee, Wisconsin
October 20, 2000

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Balance Sheets

	December 31,	
	2001	2000
	(in thousands, except share and per share amounts)	
Assets		
Current assets:		
Cash and cash equivalents	\$ 189,205	\$ 346,659
Marketable securities, available for sale	553,997	467,402
Accounts receivable	20,265	33,906
Prepaid expenses	6,636	3,494
Other current assets	5,989	5,970
Total current assets	776,092	857,431
Restricted cash	26,190	14,713
Property and equipment, net	80,377	43,961
Investments	26,433	7,426
Other assets	16,039	17,605
Total assets	\$ 925,131	\$ 941,136
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 11,628	\$ 8,438
Accrued expenses and other current liabilities	31,381	23,107
Accrued interest	4,467	4,911
Deferred revenue	39,498	28,329
Obligations under capital leases and other obligations	4,579	5,071
Total current liabilities	91,553	69,856
Obligations under capital leases and other obligations, excluding current portion	8,026	12,269
Deferred revenue, excluding current portion	35,201	—
Convertible subordinated notes	315,000	345,000
Total liabilities	449,780	427,125
Commitments and contingencies (Notes L and R)		
Stockholders' equity:		
Preferred stock, \$0.01 par value; 1,000,000 shares authorized; none issued and outstanding at December 31, 2001 and 2000, respectively	—	—
Common stock, \$0.01 par value; 200,000,000 shares authorized; 75,055,160 and 73,473,872 shares issued and outstanding at December 31, 2001 and 2000, respectively	751	735
Additional paid-in capital	778,018	757,522
Deferred compensation, net	(20)	(174)
Accumulated other comprehensive income	11,134	4,227
Accumulated deficit	(314,532)	(248,299)
Total stockholders' equity	475,351	514,011
Total liabilities and stockholders' equity	\$ 925,131	\$ 941,136

The accompanying notes are an integral part of the consolidated financial statements.

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statement of Operations

	Years Ended December 31,		
	2001	2000	1999
	(In thousands, except per share data)		
Revenues:			
Royalties	\$ 11,119	\$ 12,361	\$ 8,398
Product sales	59,921	52,437	44,208
Service revenues	27,466	20,245	12,911
Collaborative and other research and development revenues	68,984	68,239	43,370
Total revenues	167,490	153,282	108,887
Costs and expenses:			
Royalty payments	3,786	4,134	3,108
Cost of product sales	25,242	31,127	27,237
Cost of service revenues	10,601	8,357	4,236
Research and development	148,673	101,093	85,029
Sales, general and administrative	47,337	46,014	40,918
Merger related costs	23,654	—	—
Total costs and expenses	259,293	190,725	160,528
Loss from operations	(91,803)	(37,443)	(51,641)
Interest income	45,133	33,312	12,954
Interest expense	(19,318)	(11,653)	(1,704)
Debt conversion expense	—	(14,375)	—
Other, net	(2,433)	(1,420)	(763)
Loss before cumulative effect of changes in accounting principles and extraordinary items	(68,421)	(31,579)	(41,154)
Cumulative effect of changes in accounting principle—revenue recognition (Note C)	(25,901)	(3,161)	—
Cumulative effect of change in accounting principle—derivatives (Note H)	17,749	—	—
Extraordinary gain on early extinguishment of debt (Note K)	10,340	—	—
Net loss	\$(66,233)	\$(34,740)	\$(41,154)
Basic and diluted net loss per common share before cumulative effects of changes in accounting principles and extraordinary gain . .	\$ (0.92)	\$ (0.47)	\$ (0.66)
Cumulative effect of changes in accounting principle revenue recognition—basic and diluted	(0.35)	(0.04)	—
Cumulative effect of change in accounting principle derivatives—basic and diluted	0.24	—	—
Extraordinary gain on early extinguishment of debt—basic and diluted	0.14	—	—
Basic and diluted net loss per common share	\$ (0.89)	\$ (0.51)	\$ (0.66)
Basic and diluted weighted average number of common shares outstanding	74,464	67,682	62,602
Unaudited pro forma amounts assuming the 2001 accounting change relating to revenue recognition is applied retroactively (Note C):			
Net loss	\$ (40,332)	\$ (45,860)	\$ (38,234)
Basic and diluted net loss per common share	\$ (0.54)	\$ (0.68)	\$ (0.61)

The accompanying notes are an integral part of the consolidated financial statements.

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Stockholders' Equity and Comprehensive Loss

	Common Stock Shares Amount	Additional Paid-In Capital	Deferred Compensation	Accumulated Other Comprehensive Income (Loss) (in thousands)	Accumulated Deficit	Total Stockholders' Equity	Comprehensive Income (Loss)
Balance, December 31, 1998	62,317	\$459,196	\$(2,408)	\$ 654	\$(172,009)	\$286,056	\$ (1,721)
Net change in unrealized holding gains/(losses) on marketable securities				(1,721)		(1,721)	48
Translation adjustments				48		(41,154)	(41,154)
Net loss							<u>\$(42,827)</u>
Comprehensive loss							<u>\$(42,827)</u>
Issuances of common stock:							
Benefit plans	917	7,672				7,681	
Equity compensation for services rendered		120				120	
Amortization of deferred compensation		(577)	1,464			887	
Balance, December 31, 1999	63,234	466,411	(944)	(1,019)	(213,163)	251,917	\$ 5,762
Net change in unrealized holding gains/(losses) on marketable securities				5,762		5,762	(516)
Translation adjustments				(516)		(516)	(34,740)
Net loss							<u>\$(29,494)</u>
Comprehensive loss							<u>\$(29,494)</u>
Issuances of common stock:							
Benefit plans	5,900	120,832				120,891	
Convertible subordinated notes	4,340	170,040				170,084	
Equity compensation for services rendered		372				372	
Amortization of deferred compensation		(133)	770			637	
Adjustment for change in Pan Vera's year end					(396)	(396)	
Balance, December 31, 2000	73,474	757,522	(174)	4,227	(248,299)	514,011	\$ 7,218
Net change in unrealized holding gains/(losses) on marketable securities				7,218		7,218	(311)
Translation adjustments				(311)		(311)	(66,233)
Net loss							<u>\$(59,326)</u>
Comprehensive loss							<u>\$(59,326)</u>
Issuances of common stock:							
Benefit plans	1,581	19,637				19,653	
Equity compensation for services rendered		320				320	
Tax benefit of disqualifying disposition		539				539	
Amortization of deferred compensation			154			154	
Balance, December 31, 2001	75,055	\$778,018	\$ (20)	\$ 11,134	\$(314,532)	\$475,351	

The accompanying notes are an integral part of the consolidated financial statements.

VERTEX PHARMACEUTICALS
Consolidated Statements of Cash Flows

	Years Ended December 31,		
	2001	2000	1999
	(In thousands)		
Cash flows from operating activities:			
Net loss	\$ (66,233)	\$ (34,740)	\$(41,154)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	17,964	12,792	9,671
Non-cash based compensation expense	474	1,009	1,007
Write-down of marketable securities and investments	2,100	1,369	—
Other non-cash items, net	31	123	(245)
Loss on disposal of property and equipment	1,107	0	0
Realized (gains)/losses on marketable securities	(3,081)	270	655
Equity in losses of unconsolidated subsidiary	662	550	724
Adjustment for PanVera year end	—	(396)	—
Extraordinary gain on early extinguishment of debentures	(10,340)	—	—
Cumulative effects of changes in accounting principles	8,152	3,161	—
Changes in operating assets and liabilities:			
Accounts receivable	13,641	(21,639)	(5,676)
Prepaid expenses	(3,142)	(514)	(833)
Other current assets	63	(3,163)	(723)
Accounts payable	3,190	1,538	1,053
Accrued expenses and other current liabilities	7,313	8,053	5,677
Accrued interest	(444)	4,840	51
Deferred revenue	20,469	12,935	9,532
Net cash used in operating activities	<u>(8,074)</u>	<u>(13,812)</u>	<u>(20,261)</u>
Cash flows from investing activities:			
Purchases of marketable securities	(1,252,781)	(1,403,737)	(376,864)
Sales and maturities of marketable securities	1,176,186	1,117,196	437,582
Expenditures for property and equipment	(53,899)	(18,033)	(18,038)
Restricted cash	(11,477)	2,399	(13,701)
Investments and other assets	(3,116)	(5,284)	(4,745)
Net cash (used in) provided by investing activities	<u>(145,087)</u>	<u>(307,459)</u>	<u>24,234</u>
Cash flows from financing activities:			
Private placement of common stock, net	—	70,940	—
Issuances of common stock, net	19,653	49,951	7,646
Repurchase of convertible debentures	(18,900)	—	—
Proceeds from sale of convertible subordinated notes, net of costs of \$16,038	—	503,962	—
Proceeds from notes payable, capital lease and loan obligations	—	1,120	6,795
Principal payments on capital leases and other obligations	(4,735)	(5,544)	(5,052)
Net cash (used in) provided by financing activities	<u>(3,982)</u>	<u>620,429</u>	<u>9,389</u>
Effect of changes in exchange rates on cash	(311)	(516)	48
Net increase (decrease) in cash and cash equivalents	(157,454)	298,642	13,410
Cash and cash equivalents—beginning of period	346,659	48,017	34,607
Cash and cash equivalents—end of period	<u>\$ 189,205</u>	<u>\$ 346,659</u>	<u>\$ 48,017</u>
Supplemental disclosure of cash flow information:			
Cash paid for interest	\$ 18,244	\$ 20,390	\$ 1,611
Cash paid for taxes	\$ 156	\$ 360	\$ —
Non-cash financing activities:			
Property acquired under capital leases	\$ —	\$ 591	\$ 1,701
Conversion of convertible subordinated notes, net of unamortized deferred debt issuance costs of \$4,917	\$ —	\$ 170,083	\$ —

The accompanying notes are an integral part of the consolidated financial statements.

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements

A. The Company

Vertex Pharmaceuticals Incorporated (“Vertex” or the “Company”) is a global biotechnology company that seeks to discover, develop, and commercialize major pharmaceutical products independently and with collaborators. The Company has four facilities worldwide with over 1000 employees. The facilities are located in Cambridge, MA, Madison, WI, San Diego, CA and Abingdon, UK. Chemogenomics, the Company’s proprietary, systematic, genomics-based platform, is designed to accelerate the discovery of new drugs and to expand intellectual property coverage of drug candidate compounds and classes of related compounds. This approach, which targets gene families, has formed the basis for successful drug discovery and for the advancement of drug candidates by Vertex and its collaborators. We are developing several drug candidates in commercial collaborations that retain rights to downstream product revenue for the Company. Vertex has more than twelve drug candidates in development to treat viral diseases, cancer, autoimmune and inflammatory diseases and neurological disorders. The Company’s first approved product is Agenerase® (amprenavir), an HIV protease inhibitor, which Vertex co-promotes with GlaxoSmithKline. The Company earns a royalty on sales of Agenerase. Agenerase has received approval in 34 countries worldwide, including the United States, the 15 member states of the European Union, and Japan, where the drug is sold under the trade name Prozei™. The Company expects to incur operating losses for the foreseeable future, as a result of expenditures for its research and development programs.

On July 18, 2001, the Company completed a merger with Aurora Biosciences Corporation (“Aurora”). Aurora specializes in industry-leading assay development, screening and cell biology capabilities. Aurora generates revenue primarily from product sales and services related to assay development and specialized screening services and systems. The Company acquired all of Aurora’s outstanding common stock in a tax-free, stock for stock transaction, for approximately 14.1 million shares of Vertex common stock. The merger was accounted for as a pooling of interests.

On March 1, 2001, Aurora completed a merger with PanVera Corporation (“PanVera”). PanVera is a biotechnology company engaged in the development, manufacture and worldwide supply of proteins for evaluation as targets and drug screening assays for high-throughput screening. Aurora acquired all of PanVera’s outstanding common stock in a tax-free, stock for stock transaction. The merger has been accounted for as a pooling of interests. All references to “Aurora” refer to the combined company of Aurora and PanVera.

The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, rapid technological change and competition, dependence on key personnel, uncertainty of protection of proprietary technology, clinical trial uncertainty, dependence on collaborative partners, share price volatility, the possible need to obtain additional funding, uncertainties relating to pharmaceutical pricing and reimbursement, limited experience in manufacturing, sales and marketing, potential product liability and the need for compliance with government regulations.

B. Accounting Policies

Basis of Presentation

The consolidated financial statements reflect the operations of the Company and its wholly owned subsidiaries. The mergers with Aurora and PanVera have been accounted for as a pooling of interests under Accounting Principles Board Opinion No. 16, “Business Combinations” (“APB 16”). Accordingly, all prior period consolidated financial statements presented have been restated to include the combined results of operations, financial position and cash flows of Aurora and PanVera as though the mergers had been in effect since the inception of Aurora and PanVera. All significant intercompany balances and transactions have been eliminated.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

B. Accounting Policies (Continued)

Prior to the merger, PanVera's fiscal year end was September 30. In recording the business combination, PanVera's results of operations for the fiscal years ended September 30, 2000 and 1999 have been combined with the Company's results of operations for the fiscal years ended December 31, 2000 and 1999. In accordance with APB 16, PanVera's results of operations and cash flows for the three month period ended December 31, 2000 have been added directly to the Company's accumulated deficit and cash flows at December 31, 2000, and are excluded from reported fiscal 2000 consolidated results of operations. PanVera's revenue and net loss for the three months ended December 31, 2000 was \$3,005,000 and \$396,000, respectively. Included in PanVera's results of operations for the three months ended December 31, 2000 were merger related costs of approximately \$467,000. The combined balance sheet at December 31, 2000 includes PanVera's balance sheet at December 31, 2000.

Reclassification in the Preparation of Financial Statements

Certain amounts in prior years' financial statements have been reclassified to conform to the current presentation. These reclassifications had no effect on the reported net loss.

Use of Estimates

The preparation of consolidated financial statements in conformity with generally accepted accounting principles requires management to make certain estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reported periods. Significant estimates in these consolidated financial statements include useful lives for depreciation and amortization, warranty reserves, collectibility of accounts receivable, estimated fair value of equity instruments and whether any decline in such fair value is other-than-temporary and estimates of cost to completion under long-term production contracts applying percentage of completion accounting. Actual results could differ from those estimates.

Cash and Cash Equivalents

Cash equivalents, which are money market funds and debt securities, are valued at cost plus accrued interest. The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents. Changes in cash and cash equivalents may be affected by shifts in investment portfolio maturities as well as by actual cash receipts and disbursements.

Marketable Securities

Marketable securities consist of investments in high grade corporate bonds, asset-backed securities and U.S. government agency securities and are classified as available for sale. Since these securities are available to fund current operations, they are classified as current assets on the balance sheet. Marketable securities are stated at fair value with unrealized gains and losses included as a component of accumulated other comprehensive income (loss), which is a separate component of stockholders' equity, until realized. The fair value of these securities is based on quoted market prices. If a decline in the fair value is considered other-than-temporary, based on available evidence, the unrealized loss is re-classed from other comprehensive income (loss) to the consolidated statement of operations. For the years ended December 31, 2001 and 2000, the Company recorded \$600,000 and \$1,369,000, respectively, in charges to write down certain marketable securities because the decline in value was considered

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

B. Accounting Policies (Continued)

other-than-temporary. There were no write-downs in 1999. Realized gains and losses are determined on the specific identification method and are included in interest income.

Investments

Investments include long term investments recorded under both the cost and equity methods of accounting. The Company uses the equity method of accounting for investments when it has an ownership interest of 20% to 50%. When the Company holds an ownership interest of less than 20%, and does not have the ability to exercise significant influence over the investment entity's operating activities, the Company accounts for its investment using the cost method. If any adjustment to fair value reflects a decline in the value of the investment below cost, the Company considers available evidence, including the duration and extent to which the market value has been less than cost, to evaluate the extent to which the decline is other-than-temporary. If the decline is considered other-than-temporary, the cost basis of the investment is written down to fair value as a new cost basis and the amount of the write down is included in the Company's consolidated statement of operations. For the year ended December 31, 2001, the Company recorded \$1,500,000 in charges related to the write-down of an investment because the decline in the value of the investment was considered other-than-temporary.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to concentration of credit risk, consist principally of money market funds and marketable securities. The Company places these investments in highly rated financial institutions, and, by policy, limits the amounts of credit exposure to any one financial institution. These amounts at times may exceed federally insured limits. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no foreign exchange contracts, option contracts or other foreign hedging arrangements.

To date, the Company's revenue has been generated from a limited number of customers in the biotechnology and pharmaceuticals industries in the US, Europe and Japan. In 2001, the Company's revenue included transactions with each of the following customers: Novartis Pharma AG (22%) and Pfizer, Inc (17%), including Warner-Lambert, which Pfizer acquired in 2000. In 2000 the Company's revenue included significant transactions with these same two customers, Novartis (18%) and Pfizer (17%). In 1999 the Company had significant revenue transactions with Aventis S.A. (14%). The loss of such customers could have a material adverse impact on the Company.

GlaxoSmithKline, Kissei Pharmaceuticals, Co, Ltd. and Novartis Pharma AG represented approximately 20%, 15%, and 10%, respectively, of the Company's accounts receivable balance at December 31, 2001. At December 31, 2000, Pfizer represented 33% and GlaxoSmithKline represented 11% of the Company's accounts receivable balance. Management believes that credit risks associated with these collaborative partners are not significant.

Property and Equipment

Property and equipment are recorded at cost. Depreciation and amortization are provided using the straight-line method over the lesser of the lease terms or the estimated useful lives of the related assets, generally four to seven years for furniture and equipment, three to five years for computers and software and forty years for buildings. Leasehold improvements are amortized over the lesser of the useful life of the improvements or the remaining life of the lease. Major additions and betterments are

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

B. Accounting Policies (Continued)

capitalized; maintenance and repairs, which do not improve or extend the life of the respective assets, are charged to operations. When assets are retired or otherwise disposed of, the assets and related allowances for depreciation and amortization are eliminated from the accounts and any resulting gain or loss is reflected in the Company's consolidated statement of operations.

Warranty Reserve

Estimated expenses for warranty obligations in connection with instrumentation system sales are accrued as revenue is recognized. Reserve estimates are adjusted periodically to reflect actual experience.

Stock-Based Compensation

In accounting for its stock-based compensation plans, the Company applies Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees" ("APB 25") and related interpretations for all awards granted to employees. Under APB 25, provided other criteria are met, when the exercise price of options granted to employees under these plans equals the market price of the common stock on the date of grant, no compensation cost is required. When the exercise price of options granted to employees under these plans is less than the market price of the common stock on the date of grant, compensation costs are expensed over the vesting period. Subsequent changes to option terms can also give rise to compensation. For stock options granted to nonemployees, the Company recognizes compensation costs in accordance with the requirements of Statement of Financial Accounting Standards No. 123, "Accounting for Stock-Based Compensation" ("SFAS 123"). SFAS 123 requires that companies recognize compensation expense for grants of stock, stock options and other equity instruments based on fair value.

Revenue Recognition

The Company's revenue recognition policies are in accordance with the Securities and Exchange Commission's ("SEC") Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements" ("SAB 101"). The Company generates revenues through collaborative research and development agreements, assay development and screening services, product sales and royalty agreements.

Collaborative and other Research and Development Revenue

The Company's collaborative and other research and development revenue is primarily generated through collaborative research and development agreements with strategic partners for the development of small molecule drugs that address major unmet medical needs. The terms of the agreements typically include non-refundable up-front license fees, funding of research and development efforts, payments based upon achievement of certain at-risk and substantive milestones and royalties on product sales.

In the third quarter of 2001, in connection with an overall review of accounting policies concurrent with the merger with Aurora, Vertex elected to change its revenue recognition policy for collaborative and other research and development revenues from the Emerging Issues Task Force No. 91-6 ("EITF 91-6") method to the Substantive Milestone Method. Under the Substantive Milestone Method, adopted retroactively to January 1, 2001, the Company recognizes revenue from non-refundable, up-front license fees and milestones, not specifically tied to a separate earnings process, ratably over the contracted or estimated period of performance. Research funding is recognized as earned, ratably

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

B. Accounting Policies (Continued)

over the period of effort. Milestones, based on designated achievement points that are considered at risk and substantive at the inception of the collaborative contract, are recognized as earned, when the corresponding payment is reasonably assured. The Company evaluates whether milestones are at risk and substantive based on the contingent nature of the milestone, specifically reviewing factors such as the technological and commercial risk that needs to be overcome and the level of investment required.

In the fourth quarter of 2000, Vertex had changed its method of accounting for revenue recognition to the EITF 91-6 method in conjunction with the adoption of SAB 101. Under the EITF 91-6 method, adopted retroactively to January 1, 2000, the Company recognized revenue from research and development arrangements, including non-refundable upfront license fees, milestones and research and development funding, over the period of continuing involvement using the lesser of the non-refundable cash received or the result achieved using percentage of completion accounting. Where the Company had no continuing involvement, non-refundable license fees were recorded as revenue upon receipt and milestones were recorded as revenue upon achievement of the milestone by the collaborative partner.

The cumulative effect of the change in accounting principle related to revenue recognition recorded in the third quarter of 2001, retroactive to January 1, 2001, resulted in a non-cash charge to income of \$25,901,000. Prior 2001 quarterly financial results have been restated for the retroactive adoption of the Company's new revenue recognition policy to January 1, 2001.

The cumulative effect of the change in accounting principle relating to the adoption of SAB 101 in the fourth quarter of 2000, retroactive to January 1, 2000, resulted in a non-cash charge to income of \$3,161,000. Prior 2000 quarterly financial results have been restated for the retroactive adoption of SAB 101 to January 1, 2000.

Product Sales

Product sales include instrumentation system sales, technology licensing and biotechnology product sales as well as commercial drug substance sales. Revenue from licenses where Vertex has continuing obligations is recognized over the period of the license. Revenue from perpetual licenses is recognized when the license is issued, provided that there are no significant continuing obligations and the payment is non-refundable and non-creditable.

Revenue from sales of commercial drug substance, biotechnology products and certain instrumentation system sales, is recognized upon shipment, when the title to the product and associated risk of loss has passed to the customer, collectibility is reasonably assured and, if applicable, upon acceptance when acceptance criteria are specified or upon expiration of the acceptance period. Sales under long-term production contracts are recognized using percentage of completion accounting, based on actual costs incurred to date compared to total estimated costs to complete. Funding for prototype instrumentation systems was recognized ratably over the terms of the agreements, which approximated costs incurred. Milestones related to delivery of the components of the prototype systems were recognized when earned, as evidenced by written acknowledgement of acceptance from the customer.

Service Revenues

Service revenues include assay development, screening services, and contracted product development. Service revenue is recognized as the services are performed or ratably over the service period if the Company believes such method will approximate the expense being incurred. Revenue from up-front fees is deferred and recognized over the service period.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

B. Accounting Policies (Continued)

Aurora has certain contracts under which it agrees to sell instrumentation systems and technology licenses, in addition to providing assay development and screening services. Each of these separable elements may be individually delivered and is not considered essential to the functionality of the others. The Company allocates revenue under such contracts to each of the separable elements based on the relative fair value of each element, which under most of our agreements approximates the stated price in the contract.

Royalty Revenue

Royalty revenue is recognized based upon actual and estimated net sales of licensed products in licensed territories as provided by the collaborative partner and is generally recognized in the period the sales occur. Differences between actual royalty revenues and estimated royalty revenues, which have not been historically significant, are reconciled and adjusted for in the quarter they become known.

Accounts receivable includes unbilled amounts on long-term production contracts totaling \$3,441,000 and \$11,666,000 at December 31, 2001 and 2000, respectively. Unbilled receivables represent amounts due from customers that will be billed at future dates in accordance with contract terms. The unbilled receivables at December 31, 2001 are expected to be billed and collected within one year.

Research and Development

All research and development costs, including amounts funded in research collaborations, are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities including salaries and benefits, facilities costs, overhead costs, clinical trial costs, contract services and other outside costs. Customer-sponsored research and development expenses totaled approximately \$69,752,000, \$52,010,000 and \$38,507,000 in 2001, 2000 and 1999, respectively. Revenue from customer-sponsored research and development totaled approximately \$68,984,000, \$68,239,000 and \$43,370,000 in 2001, 2000 and 1999, respectively. Company-sponsored research and development expenses totaled approximately \$78,921,000, \$49,083,000 and \$46,522,000 in 2001, 2000 and 1999, respectively.

Advertising

All advertising costs are expensed as incurred. During the years ended December 31, 2001, 2000 and 1999, advertising expenses totaled \$444,000, \$1,794,000 and \$2,538,000 respectively.

Income Taxes

Deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the financial statement carrying amounts and the income tax bases of assets and liabilities. A valuation allowance is applied against any net deferred tax asset if, based on the weighted available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

Debt Issuance Costs

Debt issuance costs related to expenses incurred to complete convertible subordinated debenture offerings are deferred and amortized based on the effective interest method over the term of the related debt issuance. The amortization expense is included in interest expense on the consolidated statements of operations.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

B. Accounting Policies (Continued)

Comprehensive Income (Loss)

Comprehensive income (loss) consists of net income (loss) and other comprehensive income (loss), which includes foreign currency translation adjustments and unrealized gains and losses on certain marketable securities. For purposes of comprehensive income (loss) disclosures, the Company does not record tax provisions or benefits for the net changes in foreign currency translation adjustment, as the Company intends to permanently reinvest undistributed earnings in its foreign subsidiaries.

Foreign Currency Translation

The functional currency of the Company's foreign subsidiary is the local currency. Assets and liabilities of the foreign subsidiary are remeasured into U.S. dollars at rates of exchange in effect at the end of the year. Revenue and expense amounts are remeasured using the average exchange rates for the period. Net unrealized gains and losses resulting from foreign currency remeasurement are included in other comprehensive income (loss), which is a separate component of stockholders' equity.

Basic and Diluted Loss per Common Share

Basic earnings per common share is based upon the weighted average number of common shares outstanding during the period. Diluted earnings per common share is based upon the weighted average number of common shares outstanding during the period plus additional weighted average common equivalent shares outstanding during the period when the effect is not anti-dilutive. Common equivalent shares result from the assumed exercise of outstanding stock options, the proceeds of which are then assumed to have been used to repurchase outstanding stock using the treasury stock method, and the assumed conversion of subordinated convertible notes. Common equivalent shares have not been included in the net loss per common share calculations as their effect would be anti-dilutive.

Potential common equivalent shares consist of the following at December 31, (shares in thousands):

	<u>2001</u>	<u>2000</u>	<u>1999</u>
Stock options outstanding	16,810	14,615	15,806
Weighted average exercise price	\$27.37	\$25.97	\$11.49
Convertible notes	3,414	3,739	—
Weighted average conversion price	\$92.26	\$92.26	—

Segment Information

The Company's business operations have been segregated into two reportable segments: (i) Vertex and (ii) Aurora. Vertex seeks to discover, develop, and commercialize major pharmaceutical products independently and with partners. Aurora specializes in industry-leading assay development, screening and cell biology capabilities.

New Accounting Pronouncements

In June 2001, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standard No. 141, "Business Combinations" ("SFAS No. 141"). SFAS No. 141 requires that all business combinations be accounted for under the purchase method only and that certain acquired intangible assets in a business combination be recognized as assets distinct from goodwill. SFAS No. 141 is effective for all business combinations initiated after June 30, 2001 and for all business

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

B. Accounting Policies (Continued)

combinations accounted for by the purchase method for which the date of acquisition is after June 30, 2001.

In June 2001, the FASB issued SFAS No. 142, "Goodwill and Other Intangible Assets" ("SFAS No. 142"), which requires that ratable amortization of goodwill be replaced with periodic tests of the goodwill's impairment and that intangible assets other than goodwill be amortized over their useful lives. The provisions of SFAS No. 142 are effective for fiscal years beginning after December 15, 2001, and was adopted by the Company, as required, on January 1, 2002. The Company does not expect SFAS No. 142 will have a material effect on its financial position and results of operations.

In October 2001, the FASB issued SFAS No. 144, "Accounting for the Impairment of Long-Lived Assets" ("SFAS No. 144"). SFAS No. 144 supercedes SFAS No. 121, "Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to be Disposed Of" and provides a single accounting model for long-lived assets to be disposed of. The provisions of SFAS No. 144 will be effective for fiscal years beginning after December 15, 2001. The Company does not expect SFAS No. 144 will have a material effect on its financial position and results of operations.

C. Change in Accounting Principle—Revenue Recognition

In the third quarter of 2001, in connection with an overall review of accounting policies concurrent with the merger with Aurora, Vertex elected to change its revenue recognition policy for collaborative and other research and development revenues from the EITF 91-6 method to the Substantive Milestone Method. Vertex believes this method is preferable because it is more reflective of the Company's on-going business operations and is more consistent with industry practices following the prior year implementation of SAB 101 throughout the biotechnology industry. Under the Substantive Milestone Method, adopted retroactively to January 1, 2001, the Company recognizes revenue from non-refundable up-front, license fees and milestones, not specifically tied to a separate earnings process, ratably over the contracted or estimated period of performance. Research funding is recognized as earned, ratably over the period of effort. Milestones, based on designated achievement points that are considered at risk and substantive at inception of the contract, are recognized as earned, when the corresponding payment is reasonably assured. The Company evaluates whether milestones are at risk and substantive based on the contingent nature of the milestone, specifically reviewing factors such as the technological and commercial risk that needs to be overcome and the level of investment required.

During 2000, the Company had recognized revenue from collaborative research and development arrangements in a manner consistent to that prescribed by EITF 91-6. Under that model, revenue was recognized for non-refundable license fees, milestones, and collaborative research and development funding using the lesser of the non-refundable cash received or the result achieved using percentage of completion accounting. Where the Company had no continuing involvement, non-refundable license fees were recorded as revenue upon receipt and milestones were recorded as revenue upon achievement of the milestone by the collaborative partner.

Pursuant to the 2001 change in accounting principle to the Substantive Milestone Method, Vertex recorded a one-time non-cash charge of \$25,901,000. The impact of the adoption of this new accounting policy for revenue recognition for collaborative and other research and development revenues was to defer revenue recognition for certain portions of revenue previously recognized under our collaborative agreements into future accounting periods. The results of the first two quarters of 2001 have been restated in accordance with the new revenue recognition policy. The pro forma amounts for net loss and net loss per basic and diluted common share, presented in the consolidated

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

C. Change in Accounting Principle—Revenue Recognition (Continued)

statements of operations were calculated assuming the accounting change was made retroactively to all prior periods. Included in the 2001 collaborative and other research and development revenue is \$7,748,000 of revenue that was included in the cumulative effect of the change in accounting principle. The amount of revenue to be recognized in future years that was included in the cumulative effect of the change in accounting principle is \$6,979,000, \$2,809,000, \$2,580,000 and \$5,785,000 in 2002, 2003, 2004 and thereafter, respectively.

In connection with the adoption of SAB 101 in the fourth quarter of 2000, Vertex changed its accounting for revenue recognition to the EITF 91-6 model. In 1999, prior to the adoption of SAB 101, Vertex recognized revenue from collaborative research and development arrangements as earned under the terms of the arrangements. License payments were recorded as revenue when payment was assured and contractual obligations met. Payments from contractual milestones were recognized when achieved, and product research funding was recorded on a quarterly basis, when research effort was incurred. Under the EITF 91-6 model, adopted retroactively to January 1, 2000, the Company recognized revenue from research and development arrangements, including non-refundable license fees, milestones and research and development funding, over the period of continuing involvement using the lesser of the non-refundable cash received or the result achieved using percentage of completion accounting. Where the Company had no continuing involvement, non-refundable license fees were recorded as revenue upon receipt and milestones were recorded as revenue upon achievement of the milestone by the collaborative partner. Pursuant to the adoption of SAB 101 in 2000, the Company recorded a one-time non-cash charge of \$3,161,000, representing a cumulative effect of a change in accounting principle.

D. Business Combinations

On July 18, 2001, the Company completed a merger with Aurora in a tax-free, stock for stock transaction, which has been accounted for as a pooling of interests. Each share of Aurora common stock converted into shares of newly issued Vertex common stock at a fixed ratio of 0.62 shares of Vertex common stock for each share of Aurora common stock. A total of approximately 14.1 million shares of Vertex common stock were exchanged for all of Aurora's outstanding common stock, and Aurora's outstanding stock options were converted into approximately 2.6 million options to purchase Vertex common stock, based upon the same fixed ratio.

On March 1, 2001, Aurora completed a merger with PanVera. The merger qualified as a tax-free exchange and was accounted for as a pooling of interests. A total of approximately 1.6 million shares of Aurora common stock, which converted into approximately 1.0 million shares of Vertex common stock, were exchanged for all of PanVera's outstanding stock. PanVera's outstanding stock options were converted into options to purchase approximately 260,000 shares of Aurora common stock which converted into approximately 161,000 shares of Vertex common stock.

The Company's consolidated financial statements have been restated for all periods prior to the business combinations to include the combined financial results of Vertex, Aurora and PanVera.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

D. Business Combinations (Continued)

Revenue and net income (loss) for the individual companies reported prior to the mergers were as follows (in thousands):

	<u>Six Months Ended June 30, 2001</u>	<u>Year Ended December 31, 2000</u>	<u>Year Ended December 31, 1999</u>
Revenue:			
Vertex	\$ 35,715*	\$ 78,127	\$ 50,560
Aurora	30,788	63,790	50,521
PanVera	9,129	11,365	7,806
Inter Company	(35)	—	—
Total	<u><u>\$ 75,597</u></u>	<u><u>\$153,282</u></u>	<u><u>\$108,887</u></u>
Net Income (Loss):			
Vertex	\$(51,663)*	\$(39,658)	\$(40,966)
Aurora	(826)	4,353	(209)
PanVera	996	565	21
Total	<u><u>\$(51,493)</u></u>	<u><u>\$(34,740)</u></u>	<u><u>\$(41,154)</u></u>

* Revenue and net loss for the six months ended June 30, 2001 for Vertex has been restated to reflect the adoption of the Substantive Milestone Method of revenue recognition, retroactive to January 1, 2001 (Note C).

The conforming of accounting policies of Vertex, Aurora and PanVera did not result in adjustments to net income or stockholders' equity. There were no significant intercompany transactions between the three entities for the years ended December 31, 2000 and 1999.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

E. Marketable Securities

A summary of cash equivalents and available-for-sale securities is shown below (in thousands):

<u>December 31, 2001</u>	<u>Amortized Cost</u>	<u>Gross Unrealized Gains</u>	<u>Gross Unrealized Losses</u>	<u>Fair Value</u>
Cash and cash equivalents				
Cash and money market funds	\$183,810			\$183,810
Corporate debt securities	5,395			5,395
Total cash and cash equivalents	<u>\$189,205</u>			<u>\$189,205</u>
Marketable securities				
Total equity securities	\$ 931	\$ 52	\$ 68	\$ 915
US government securities				
Due within 1 year	26,016			26,199
Due within 1 to 5 years	94,342			95,726
Total US government securities	<u>120,358</u>	<u>1,574</u>	<u>7</u>	<u>121,925</u>
Corporate debt securities				
Due within 1 year	196,600			199,828
Due within 1 to 5 years	224,199			231,329
Total corporate debt securities	<u>420,799</u>	<u>10,422</u>	<u>64</u>	<u>431,157</u>
Total marketable securities	<u>\$542,088</u>	<u>\$12,048</u>	<u>\$139</u>	<u>\$553,997</u>
Total cash, cash equivalents and marketable securities	<u>\$731,293</u>	<u>\$12,048</u>	<u>\$139</u>	<u>\$743,202</u>

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

E. Marketable Securities (Continued)

<u>December 31, 2000</u>	<u>Amortized Cost</u>	<u>Gross Unrealized Gains</u>	<u>Gross Unrealized Losses</u>	<u>Fair Value</u>
Cash and cash equivalents				
Cash and money market funds	\$311,270			\$311,270
Municipal bonds	14,327			14,327
Corporate debt securities	<u>21,062</u>			<u>21,062</u>
Total cash and cash equivalents	<u>\$346,659</u>			<u>\$346,659</u>
Marketable securities				
Total equity securities	<u>\$ 631</u>			<u>\$ 631</u>
US government securities				
Due within 1 year	26,735			26,768
Due within 1 to 5 years	43,359			43,819
Due over 5 years	<u>2,003</u>			<u>1,975</u>
Total US government securities	<u>72,097</u>	<u>\$ 506</u>	<u>\$ 41</u>	<u>72,562</u>
Corporate debt securities				
Due within 1 year	85,786			85,863
Due within 1 to 5 years	297,305			301,131
Due over 5 years	<u>7,092</u>			<u>7,215</u>
Total corporate debt securities	<u>390,183</u>	<u>4,286</u>	<u>260</u>	<u>394,209</u>
Total marketable securities	<u>\$462,911</u>	<u>\$4,792</u>	<u>\$301</u>	<u>\$467,402</u>
Total cash, cash equivalents and marketable securities	<u>\$809,570</u>	<u>\$4,792</u>	<u>\$301</u>	<u>\$814,061</u>

Gross realized gains and losses for 2001 were \$3,134,000 and \$53,000, respectively. Gross realized gains and losses for 2000 were \$69,000 and \$339,000, respectively. Gross realized gains and losses for 1999 were \$106,000 and \$761,000, respectively. Maturities stated are effective maturities.

F. Restricted Cash

At December 31, 2001 and 2000, the Company held \$26,190,000 and \$14,713,000 in restricted cash, respectively. At December 31, 2001 the balance was comprised of \$26,087,000 held in deposit with certain banks predominantly to collateralize conditional, standby letters of credit in the names of the respective landlords in accordance with certain operating lease agreements, and \$103,000 in connection with a Variable Rate Demand Industrial Revenue Bond held by the Company. At December 31, 2000 the balance was comprised of \$10,121,000 restricted in connection with certain operating lease agreements for facilities and \$4,592,000 in connection with a Variable Rate Demand Industrial Revenue Bond.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

G. Property and Equipment

Property and equipment consist of the following at December 31 (in thousands):

	<u>2001</u>	<u>2000</u>
Furniture and equipment	\$ 47,910	\$26,971
Leasehold improvements	48,132	24,511
Equipment under capital leases	26,288	27,245
Computers	11,351	6,908
Software	8,057	6,443
Building	5,960	—
Construction in process	1,578	5,004
Total property and equipment, gross	<u>149,276</u>	<u>97,082</u>
Less accumulated depreciation and amortization	<u>68,899</u>	<u>53,121</u>
Total property and equipment, net	<u>\$ 80,377</u>	<u>\$43,961</u>

Depreciation expense for the years ended December 31, 2001, 2000 and 1999 was \$16,385,000, \$11,798,000 and \$9,576,000, respectively. The accumulated depreciation and amortization of equipment under capital leases was \$25,025,000 and \$26,957,000 at December 31, 2001 and 2000, respectively. Assets under capital leases collateralize the related lease obligations.

H. Investments

In February 1999, Vertex restructured its investment in Altus, which was a majority owned subsidiary, so that Altus operates independently from Vertex. As part of the transaction, Vertex provided Altus \$3,000,000 of cash and surrendered its shares in Altus preferred stock in exchange for two new classes of preferred stock and warrants. Vertex had a 23.5% equity investment in Altus with a balance sheet value of approximately \$1,726,000 at December 31, 2000. For the years ending December 31, 2000 and December 31, 1999, Vertex recorded \$550,000 and \$724,000, respectively, as its share of Altus' losses under the equity method of accounting. Vertex does not have any revenue related or other significant operational contracts with Altus.

In September and November of 2001, Altus underwent financial restructurings, which reduced Vertex's relative ownership in Altus to approximately 14% and 11% on the respective dates. Accordingly, effective September 28, 2001, Vertex accounts for its investment in Altus using the cost method. For the period from January 1, 2001 through September 28, 2001, Vertex recorded \$662,000 as its share of Altus' losses under the equity method of accounting.

In the third quarter of 2001, Vertex adopted Derivative Implementation Group Issue No. A17, "Contracts that Provide for Net Share Settlement" ("DIG A17"). Subsequent to the issuance of SFAS No. 133, "Accounting for Certain Derivative Instruments and Certain Hedging Activities," the FASB established the Derivatives Implementation Group to address and interpret practice issues relating to that standard. On April 10, 2001, the FASB published DIG A17 relating to contracts that provide for net share settlement, including warrants of a privately held company. Pursuant to the adoption of DIG A17 on July 1, 2001, Vertex recorded a \$17,749,000 cumulative effect of a change in accounting principle to reflect the value of warrants held in Altus as income with a corresponding increase to Investments. The valuation of the warrants was determined based on an independent appraisal that used the Black-Scholes option pricing model to value the warrants. Significant assumptions used in the Black-Scholes model included the fair value of Altus' common stock which was based on a valuation of

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

H. Investments (Continued)

Altus using projected discounted cash flows and comparable market values using multiples of revenue, volatility of 70%, risk free interest rates between 4.9% to 5.6% and warrant terms per the agreements ranging from 3.5 to 11.6 years. As of September 30, 2001, the warrants no longer qualified as derivatives under DIG A17 due to changes in the terms of the warrants coincident with the financial restructuring of Altus. The Company's cost basis carrying value in its outstanding equity and warrants of Altus was \$18,813,000 at December 31, 2001. The Company also held investments at cost in other privately held companies at December 31, 2001 and 2000.

I. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following at December 31 (in thousands):

	2001	2000
Research and development contract costs	\$10,716	\$ 6,417
Payroll and benefits	12,888	7,369
Professional fees	2,508	3,261
Other	5,269	6,060
	\$31,381	\$23,107

J. Capital Leases and Other Obligations

At December 31, 2001, long-term capital lease, loan and other obligations were due as follows (in thousands):

Year ended December 31,	Capital Leases	Other Obligations	Total
2002	\$2,945	\$1,850	\$4,795
2003	1,028	1,103	2,131
2004	101	240	341
2005	—	255	255
2006	—	245	245
Thereafter	—	5,105	5,105
Total minimum lease and loan payments	4,074	8,798	12,872
Less amount representing interest payments	267	—	267
Present value of minimum lease and loan payments	3,807	8,798	12,605
Less current portion	2,729	1,850	4,579
	\$1,078	\$6,948	\$8,026

Capital Lease Obligations

The Company leases certain equipment and improvements under capital leases, which expire at various dates through June 2004.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

J. Capital Leases and Other Obligations (Continued)

Other Obligations:

Loan Agreements

During 1998, the Company financed assets under a master loan agreement with a cost of \$1,574,000, \$1,506,000 and \$1,005,000, with interest rates of 7.89%, 8.06% and 8.08%, respectively. During 1997, the Company financed assets under a master loan agreement with a cost of \$676,000 and \$1,137,000, with interest rates of 8.59% and 8.38%, respectively. The Company has certain equipment with a net book value of \$1,407,000 designated as collateral under these agreements at December 31, 2001. These agreements have a term of five years, and require that the Company maintain a certain level of cash and investments. The carrying value of these loan obligations at December 31, 2001 and 2000 approximates fair value.

Promissory Note

In July 1997 the Company re-purchased shares of its common stock from a common stockholder by making a cash payment and issuing a promissory note. Interest is imputed at 4.91%. The balance of the note is \$274,000 at December 31, 2001. Payments of principal and interest are due in quarterly installments through July 1, 2002.

Variable Rate Demand Bonds

In October 1998, the City of Madison, Wisconsin ("City") issued \$6,300,000 of Variable Rate Demand Industrial Revenue Bonds, Series 1998 and then loaned the proceeds to the Company. The Company utilized the proceeds to finance the construction of a new laboratory, production and office facility in Madison, Wisconsin, which the Company began occupying in June 2001. Terms of the loan agreement are subject to the terms of the bonds. The loan bears interest payable monthly at a rate that is the lesser of a variable rate based upon the prevailing market conditions required to resell the bonds at par value, or 12%. Variable rate adjustments are made at specified periodic determination dates. The interest rate on the bonds may be converted to a fixed rate at the option of the Company. At December 31, 2001, the variable rate of interest was 1.85%. Interest incurred in 2001, 2000 and 1999 was \$285,000, \$386,000 and \$281,000, respectively. Interest capitalized, during construction in 2001 and 2000, was \$106,000 and \$9,375, respectively. No interest was capitalized during 1999. Principal payments are due in annual installments beginning in October 2002 through October 2018.

As a condition of the sale of the aforementioned Variable Rate Demand Industrial Revenue Bonds, the Company entered into an irrevocable letter of credit with a bank. As security for the bonds, a replacement letter was obtained in June 2000 for an initial five year term with annual extensions thereafter through October 15, 2001. The letter of credit is secured by a General Business Security Agreement, subject to certain financial covenants.

Line of Credit Agreements

At December 31, 2001, the Company had available on demand a \$1 million line of credit with a bank. The interest rate on outstanding borrowings is 1.9% over the thirty day LIBOR rate. Borrowings are limited to specified percentages of eligible accounts receivable and inventory. There were no borrowings outstanding on this line of credit during 2001.

At December 31, 2001, the Company also had available a \$1 million transaction note subject to the same terms and conditions as the line of credit. There were no borrowings outstanding on this note during 2001.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

J. Capital Leases and Other Obligations (Continued)

Both the line of credit and transaction note are cross-collateralized with a letter of credit.

In December 1999, the Company obtained a line of credit allowing for borrowings in aggregate of up to \$20,000,000 for equipment and leasehold improvement expenditures. No amounts were drawn down against the line of credit and it expired unused in 2001.

K. Convertible Subordinated Notes

On March 14, 2000, the Company issued \$175,000,000 of 5% Convertible Subordinated Notes due March 2007 ("March Notes"). The notes were convertible, at the option of the holder, into common stock at a price equal to \$40.32 per share, subject to adjustment under certain circumstances. The deferred costs associated with issuance of the March Notes were \$5,340,000, of which \$423,000 was amortized to interest expense in 2000.

On September 15, 2000, the Company announced the call for redemption of its March Notes. By October 4, 2000, all of the March Notes were converted by holders into 4,340,260 shares of common stock at a price of \$40.32 per share. The Company reclassified \$4,917,000 of related unamortized deferred debt issuance costs to stockholders' equity as part of the conversion. In connection with the call for redemption, the holders of the March Notes were entitled to a "make-whole" payment of \$82.14 per \$1,000 principal amount of notes, which resulted in a one-time charge to earnings of \$14,375,000 in the third quarter of 2000. The "make-whole" payment was paid in cash in the fourth quarter of 2000.

On September 19, 2000, the Company issued \$345,000,000 of 5% Convertible Subordinated Notes due September 2007 ("September Notes"). The September Notes are convertible, at the option of the holder, into common stock at a price equal to \$92.26 per share, subject to adjustment under certain circumstances. The September Notes bear an interest rate of 5% per annum, and the Company is required to make semi-annual interest payments on the outstanding principal balance of the notes on March 19 and September 19 of each year. The September Notes are redeemable by the Company at any time on or after September 19, 2003 at specific redemption prices if the closing price of the Company's common stock exceeds 120% of the conversion price then in effect for at least 20 trading days within a period of 30 consecutive trading days. Before September 19, 2003 the Company may redeem the notes at a redemption price equal to the principal amount of notes, plus accrued and unpaid interest, if any, and a specified additional payment amount, if the closing price of the Company's common stock exceeds 150% of the conversion price then in effect for at least 20 trading days within a period of 30 consecutive trading days. The deferred costs associated with the sale of the convertible notes, which are classified as long-term other assets, were \$10,698,000 of which \$1,498,000 and \$428,000 was amortized to interest expense in 2001 and 2000, respectively.

In October 2001, the Company re-purchased \$30,000,000 in principal amount of its September Notes for cash consideration of \$18,900,000. As a result of this transaction the Company recorded an extraordinary gain on the early extinguishment of debt of \$10,340,000, net of \$760,000 of deferred debt costs in the fourth quarter of 2001. At December 31, 2001, the September Notes had an outstanding balance of \$315,000,000 and a fair value of \$212,121,000, as obtained from a quoted market source.

L. Commitments

The Company leases its facilities and certain equipment under non-cancelable operating leases. The Company's leases have terms through the year 2017. In January of 2001, the Company entered into a lease agreement to lease approximately 275,000 square feet of laboratory and office space

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

L. Commitments (Continued)

presently under construction. The Company will begin paying rent on this new facility in March 2003. The lease will expire in 2017 with the option to extend the lease for two consecutive terms of ten years each, ultimately expiring in 2037. The Company's future minimum commitments under this lease are included in the table below.

At December 31, 2001, future minimum commitments under facility operating leases with non-cancelable terms of more than one year are as follows (in thousands):

<u>Year</u>	<u>Operating Leases</u>
2002	\$ 18,706
2003	33,481
2004	32,916
2005	32,804
2006	28,902
Thereafter	<u>255,796</u>
Total minimum lease payments	<u>\$402,605</u>

Rental expense was \$15,447,000, \$8,892,000 and \$8,139,000 for the years ended December 31, 2001, 2000 and 1999, respectively.

The Company has future contractual commitments in connection with its research and development programs. For the years 2002, 2003, 2004 and 2005 the amounts committed under these contracts are \$6,859,000, \$3,924,000, \$2,209,000 and \$865,000, respectively.

M. Income Taxes

For the year ended December 31, 2001, the Company provided approximately \$630,000 for income taxes which was recorded in Other, net on the Consolidated Statement of Operations. The provision principally relates to certain foreign and state tax obligations, in addition to recording a valuation allowance for certain deferred tax assets acquired in the merger with Aurora. The Company's federal statutory income tax rate for 2001, 2000 and 1999 was 34%. The Company has incurred losses from operations but has not recorded an income tax benefit for 2001, 2000 and 1999 as the Company has recorded a valuation allowance against its net operating losses and other net deferred tax assets due to uncertainties related to the realizability of these tax assets.

Deferred tax liabilities and assets are determined based on the difference between financial statement and tax bases using enacted tax rates in effect for the year in which the differences are expected to reverse. The components of deferred taxes at December 31 were as follows (in thousands):

	<u>2001</u>	<u>2000</u>
Deferred Tax Assets:		
Net operating loss	\$ 151,168	\$ 137,723
Tax credits carryforward	26,512	25,304
Property, plant and equipment	3,984	1,931
Deferred revenue	7,442	4,128
Capitalized research and development	33,239	28,879
Other	1,918	1,308
Gross deferred tax asset	<u>224,263</u>	<u>199,273</u>
Valuation allowance	(224,263)	(199,076)
Net deferred tax asset	<u>\$ —</u>	<u>\$ 197</u>

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

M. Income Taxes (Continued)

Of the \$224,263,000 valuation allowance at December 31, 2001, \$95,027,000 relates to deductions for nonqualified stock options, which will be credited to additional paid-in capital, if realized.

For federal income tax purposes, as of December 31, 2001, the Company has net operating loss carryforwards of approximately \$384,338,000 and \$17,597,000 of tax credits, which may be used to offset future income. These operating loss carryforwards expire beginning in 2005, and the tax credit carryforwards begin to expire in 2004. A valuation allowance has been established for the full amount of the 2001 deferred tax asset since it is more likely than not that the deferred tax asset will not be realized.

N. Common and Preferred Stock

Common Stock

In August 2000, the Company effected a two-for-one stock split of all common stock in the form of a stock dividend. All common stock share and per share amounts in these consolidated financial statements have been restated to reflect this stock split.

Stock Option Plans

The Company has a 1991 Stock Option Plan (the "1991 Plan"), a 1994 Stock and Option Plan (the "1994 Plan") and a 1996 Stock and Option Plan (the "1996 Plan"). Stock options may be granted under the Plans either as options intended to qualify as "incentive stock options" ("ISOs") under the Internal Revenue Code or as non-qualified stock options ("NQSOs"). Under the 1991 Plan, stock options may be granted to employees (including officers and directors who are employees) and to consultants of the Company (NQSOs only). Under the 1994 Plan and the 1996 Plan, stock rights, which may be (i) ISOs when Internal Revenue Code requirements are met, (ii) NQSOs, or (iii) shares of common stock or the opportunity to make a direct purchase of shares of common stock ("Stock Awards"), may be granted to employees (including officers and directors who are employees, consultants, advisors and non-employee directors (NQSOs and stock awards only). Under the 1991 and 1994 Plans ISOs may be granted at a price not less than the fair market value of the common stock on the date of the grant, and NQSOs may be granted at an exercise price established by the Compensation Committee of the Board of Directors, which may be less than, equal to or greater than the fair value of the common stock on the date of the grant. Stock options granted under the 1996 Plan may not be granted at a price less than the fair market value of the common stock on the date of grant. Vesting periods for all plans are generally four or five years, and are determined by the Compensation Committee. ISOs granted under the Plans must expire not more than ten years from the date of grant.

In July 2001, in connection with the acquisition of Aurora, the Company assumed the obligations under the Aurora 1996 Stock Plan (the "Aurora Stock Plan"), the 1993 Stock Plan of PanVera Corporation (the "PanVera Plan") and certain non-plan stock option agreements ("Non-Plan Stock Option Agreements") under which 2,393,000, 109,000, 3,000 shares of Vertex's common stock, respectively, were reserved for issuance at December 31, 2001.

The Aurora Stock Plan provides for the granting of ISOs and stock appreciation rights to employees and NQSOs and stock purchase rights to employees, directors and consultants. The exercise price of ISOs must be equal to the fair market value of the Company's common stock on the date of grant, and the exercise price of NQSOs may be no less than 85% of the fair market value of the Company's common stock on the date of grant. The PanVera Plan provides for the granting of ISOs to employees of PanVera and the exercise price must be equal to the fair market value of the Company's

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

N. Common and Preferred Stock (Continued)

common stock on the date of grant. Vesting periods for the Aurora Stock Plan and Pan Vera Plan are generally four years and options expire not more than ten years from the date of grant.

The Company has reserved 8,000,000 shares under the 1991 Plan and 1994 Plan. The 1996 Plan reserved an additional 16,000,000 shares, of which 5,500,000 were reserved during 2001. At December 31, 2001, the Company had a total of 3,108,000 shares of common stock available for future grant under its 1991, 1994 and 1996 stock option plans. No shares remain available for grant under the Aurora Stock Plan, the PanVera Plan or Non-Plan Stock Option Agreements.

Consolidated stock option activity for the years ended December 31, 2001, 2000 and 1999 is as follows (shares in thousands):

	2001		2000		1999	
	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price
Outstanding at beginning of year	14,615	\$25.97	15,806	\$11.49	13,515	\$10.88
Granted	4,451	28.98	3,703	67.79	3,468	13.05
Exercised	(1,401)	11.65	(4,446)	10.25	(636)	7.19
Canceled	(855)	38.58	(448)	16.51	(541)	12.31
Outstanding at end of year	<u>16,810</u>	<u>\$27.37</u>	<u>14,615</u>	<u>\$25.97</u>	<u>15,806</u>	<u>\$11.49</u>
Options exercisable at year-end	7,476	\$19.04	5,874	\$11.56	7,532	\$ 9.99
Weighted average fair value of options granted during the year:		\$14.97		\$37.04		\$ 6.03

The fair value of each option granted under the 1991, 1994 and 1996 plans during 2001, 2000 and 1999 was estimated on the date of grant using the Black-Scholes option pricing model with the following weighted average assumptions:

	2001	2000	1999
Expected life (years)	5.50	5.50	5.50
Expected volatility	58.00%	58.00%	45.00%
Risk free interest rate	4.86%	5.63%	6.20%
Dividend yield	—	—	—

The fair value of each option granted under the Aurora Stock Plan, PanVera Plan and Non-plan Stock Option Agreements during 2001, 2000 and 1999 was estimated on the date of grant using the Black-Scholes option pricing model with the following weighted average assumptions:

	2001	2000	1999
Expected life (years)	5.50	5.00	5.00
Expected volatility	93.00%	100.00%	60.00%
Risk free interest rate	4.35%	4.69%	6.57%
Dividend yield	—	—	—

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

N. Common and Preferred Stock (Continued)

The following table summarizes information about stock options outstanding and exercisable at December 31, 2001 (shares in thousands):

Range of Exercise Prices	Options Outstanding			Options Exercisable	
	Number Outstanding	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
\$0.15-\$9.50	2,279	3.34	\$ 7.66	2,175	\$ 7.61
9.68-12.22	1,262	6.85	10.34	765	10.33
12.25-13.11	1,948	7.82	13.05	712	13.01
13.17-13.67	2,014	6.39	13.64	1,285	13.64
13.69-20.91	1,957	6.06	16.33	1,509	15.95
20.97-24.66	2,812	9.87	24.61	29	23.21
24.69-58.88	1,939	9.05	41.56	366	47.58
59.37-70.75	2,140	8.91	70.13	482	69.90
71.62-197.59	459	8.56	97.86	153	99.62
\$0.15-\$197.59	16,810	7.41	\$27.37	7,476	\$19.04

Stock Based Compensation

The Company records and amortizes over the related vesting periods deferred compensation representing the difference between the exercise price of stock options granted or the price per share of restricted stock issued and the fair value of the Company's common stock at the date of grant or issuance. Amortization of deferred compensation expense of \$154,000, \$637,000 and \$887,000 was recognized during 2001, 2000 and 1999, respectively.

Compensation cost, calculated using a Black-Scholes option pricing model, recognized in connection with the issuance of stock options to nonemployees was \$320,000, \$372,000 and \$120,000 in 2001, 2000 and 1999, respectively.

Employee Stock Purchase Plans

Under the Vertex Employee Stock Purchase Plan (the "Vertex Purchase Plan"), substantially all permanent employees may, through payroll withholdings, purchase shares of the Company's common stock at a price of 85% of the lesser of fair market value at the beginning or at the end of each six-month withholding period.

In connection with the acquisition of Aurora in July 2001, the Company assumed the obligations under the Aurora Employee Stock Purchase Plan (the "Aurora Purchase Plan"). The Aurora Purchase Plan provides for all eligible employees to purchase the Company's common stock, through payroll withholdings, at a price of 85% of the lesser of fair market value on the start date of each overlapping two-year offering period or on the date on which each semi-annual purchase period ends. The Company does not anticipate issuing any additional shares under the Aurora Purchase Plan.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

N. Common and Preferred Stock (Continued)

During 2001, 2000, and 1999 the following shares were issued to employees under the plans (shares in thousands):

	<u>2001</u>	<u>2000</u>	<u>1999</u>
Number of shares	155	289	228
Average price paid	\$20.54	\$9.50	\$7.53

Had the Company adopted SFAS 123, the weighted average fair value of each purchase right granted during 2001, 2000 and 1999 would have been \$7.45, \$5.93 and \$6.20, respectively. The fair value was estimated at the beginning of the withholding period using the Black-Scholes option-pricing model with the following weighted average assumptions:

	<u>2001</u>	<u>2000</u>	<u>1999</u>
Expected life (years)50	.50	.50
Expected volatility	58.00%	58.00%	45.00%
Risk free interest rate	2.97%	5.98%	5.72%
Dividend yield	—	—	—

Pro forma Disclosures

Had compensation expense for all stock awards been determined consistent with SFAS 123, the Company's net loss and net loss per common share would approximate the pro forma amounts below (in thousands except per share data):

		<u>2001</u>	<u>2000</u>	<u>1999</u>
Net Loss	As reported	\$ (66,233)	\$(34,740)	\$(41,154)
	Pro forma	\$(121,528)	\$(65,618)	\$(57,416)
Basic and diluted net loss per common share	As reported	\$ (0.89)	\$ (0.51)	\$ (0.66)
	Pro forma	\$ (1.63)	\$ (0.97)	\$ (0.92)

Rights

Each holder of a share of outstanding Common Stock also holds one share purchase right (a "Right") for each share of Common Stock. Each Right entitles the holder to purchase from the Company one half of one-hundredth of a share of Series A junior participating preferred stock, \$0.01 par value (the "Junior Preferred Shares"), of the Company at a price of \$135 per one half of one-hundredth of a Junior Preferred Share (the "Purchase Price"). The Rights are not exercisable until the earlier of acquisition by a person or group of 15% or more of the outstanding Common Stock (an "Acquiring Person") or the announcement of an intention to make or commencement of a tender offer or exchange offer, the consummation of which would result in the beneficial ownership by a person or group of 15% or more of the outstanding Common Stock. In the event that any person or group becomes an Acquiring Person, each holder of a Right other than the Acquiring Person will thereafter have the right to receive upon exercise that number of shares of Common Stock having a market value of two times the Purchase Price and, in the event that the Company is acquired in a business combination transaction or 50% or more of its assets are sold, each holder of a Right will thereafter have the right to receive upon exercise that number of shares of Common Stock of the acquiring company which at the time of the transaction will have a market value of two times the Purchase Price. Under certain specified circumstances, the Board of Directors of the Company may cause the Rights

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

N. Common and Preferred Stock (Continued)

(other than Rights owned by such person or group) to be exchanged, in whole or in part, for Common Stock or Junior Preferred Shares, at an exchange rate of one share of Common Stock per Right or one half of one-hundredth of a Junior Preferred Share per Right. At any time prior to the acquisition by a person or group of beneficial ownership of 15% or more of the outstanding Common Stock, the Board of Directors of the Company may redeem the Rights in whole at a price of \$0.01 per Right.

Common Stock Reserved for Future Issuance

At December 31, 2001, the Company has reserved shares of common stock for future issuance as follows (shares in thousands):

Common stock under stock option plans	19,918
Common stock under the Vertex Purchase Plan	247
Common stock under the Vertex 401(k) Plan	<u>181</u>
Total	<u><u>20,346</u></u>

O. Significant Revenue Arrangements

The Company has formed strategic collaborations with major pharmaceutical companies in the areas of drug discovery and development, assay development, screening services and instrumentation products. These collaborations include partnered research and development arrangements and system, service and licensing arrangements focused on assay development. Research and development agreements provide the Company with financial support and other valuable resources for research programs and development of clinical drug candidates, product development and marketing and sales of products. Assay development, screening services and instrumentation contracts provide contracted revenue to the Aurora business.

Collaborative Research and Development Agreements

In the Company's collaborative research and development programs the Company seeks to discover and develop novel drug candidates in conjunction with and supported by our collaborators. Collaborative research and development arrangements provide research funding over an initial contract period with renewal and termination options that vary by agreement. The agreements also include milestone payments based on the achievement or the occurrence of a designated event. The agreements may also contain development reimbursement provisions, royalty rights or profit sharing rights and manufacturing options. The terms of each agreement vary. We have entered into research and development collaborations with large pharmaceutical companies.

In May 2000, the Company and Novartis Pharma AG ("Novartis") entered into an agreement to collaborate on the discovery, development and commercialization of small molecule drugs directed at targets in the kinase protein family. Under the agreement, Novartis agreed to pay the Company approximately \$600,000,000 in pre-commercial payments, comprised of \$15,000,000 paid upon signing of the agreement, up to \$200,000,000 in product research funding over six years and up to approximately \$400,000,000 in further license fees, milestone payments and cost reimbursements. These amounts are based on the development of eight drug candidates. In addition, Novartis created a \$200,000,000 loan facility to support certain clinical studies, which the Company may draw down in increments up to \$25,000,000 for each drug candidate. The loan is interest free and Novartis will forgive the full amount of any advances if Novartis accepts the drug candidate for development under the agreement. The

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

O. Significant Revenue Arrangements (Continued)

Company will have the responsibility for drug discovery and clinical proof-of-concept testing of drug candidates. Novartis will have exclusive worldwide development, manufacturing and marketing rights to clinically and commercially relevant drug candidates that it accepts for development from the Company. Vertex will receive royalties on any products that are marketed as part of the collaboration. Subject to certain conditions, the Company will have co-promotion rights in the United States and Europe, and will retain the rights to any intellectual property resulting from the collaboration. Novartis may terminate this agreement without cause after four years upon one year's written notice. In 2001 and 2000, the Company recognized approximately \$36,723,000 and \$27,910,000, respectively, in revenue under the kinase program.

Taisho Pharmaceutical Co., LTD and Seroxo S.A.

In November 1999, the Company and Taisho Pharmaceutical Co., LTD ("Taisho") entered into an agreement to collaborate on the discovery, development and commercialization of caspase inhibitors for the treatment of cerebrovascular, cardiovascular and neurodegenerative diseases. Under the agreement, Taisho will have an option to obtain marketing rights in Japan and certain Far East markets for any compounds arising from the collaboration. Taisho agreed to pay the Company up to \$43,000,000 in pre-commercial payments, comprised of research funding and milestone payments, including \$4,500,000 for prior research costs. These amounts are based on the development of two compounds. In addition, Taisho will also pay for certain costs of developing compounds that emerge from the caspase research program. Vertex will also receive royalties on future product sales.

In December 2000, the Company and Seroxo S.A. ("Seroxo") entered into an agreement to collaborate on the discovery, development, and commercialization of caspase inhibitors. Under the agreement, the Company could receive up to \$95,000,000 in pre-commercial payments, comprised of \$5,000,000 in payments for prior research, up to \$20,000,000 in product research funding over five years and up to \$70,000,000 in further license fees and milestone payments. These amounts are based on the development of more than one drug candidate. The two companies will share development costs. The Company and Seroxo will establish a joint venture for the commercialization of products in North America, where they will share marketing rights and profits from the sale of caspase inhibitors. Seroxo will have exclusive rights to market caspase inhibitors in other territories, excluding Japan and certain other countries in the Far East, and will pay Vertex for the supply of drug substance. Seroxo has the right to terminate the agreement without cause upon 90 days written notice, effective either at September 30, 2002 or September 30, 2004.

In 2001, 2000 and 1999, the Company recognized approximately \$10,385,000, \$6,974,000 and \$3,900,000 as revenue, respectively, under the caspase program.

Aventis S.A.

In September 1999, the Company and Aventis S.A. ("Aventis"), formerly Hoechst Marion Roussel Deutschland GmbH ("HMR"), entered into an expanded agreement covering the development of pralnacasan,, an orally active inhibitor of interleukin-1 beta converting enzyme ("ICE"). Under the agreement, Aventis agreed to pay the Company \$20,000,000 for prior research costs, and up to \$62,000,000 in milestone payments for successful development by Aventis of pralnacasan in rheumatoid arthritis, the first targeted indication, as well as similar milestone payments for each additional indication. Aventis has an exclusive worldwide license to develop, manufacture and market pralnacasan, as well as an exclusive option for all other compounds discovered as part of the research collaboration between the Company and HMR that ended in 1997, under which the Company received research

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

O. Significant Revenue Arrangements (Continued)

funding. Aventis will fund the development of pralnacasan. Vertex may co-promote the product in the U.S. and Europe and will receive royalties on global sales, if any. Aventis may terminate this agreement without cause upon six months' written notice. Collaborative and other research and development revenues earned under the agreement were \$10,000,000 and \$15,000,000, in 2000 and 1999, respectively. The Company did not earn any revenue in connection with the Aventis collaboration in 2001.

Schering AG

In 1998 the Company and Schering AG, Germany ("Schering") entered into an agreement to collaborate on the research, development and commercialization of novel, orally active neurophilin ligand compounds to promote nerve regeneration for the treatment of a number of neurological diseases. Under the terms of the agreement, Schering agreed to pay the Company up to \$88,000,000 comprised of \$6,000,000 paid upon signing in September 1998, up to \$22,000,000 of product research funding over five years and \$60,000,000 of development and commercialization milestone payments. Under terms of the agreement, Vertex and Schering will have an equal role in management of neurophilin ligand research and product development. In North America, Vertex will have manufacturing rights, and Vertex and Schering will share equally in the marketing expenses and profits from commercialized compounds. In addition to having manufacturing rights in North America, the Company retains the option to manufacture bulk drug substance for sales and marketing in territories outside Europe, the Middle East and Africa. Schering will have the right to manufacture and market any commercialized compounds in Europe, the Middle East and Africa, and pay Vertex a royalty on product sales, if any. Schering has the right to terminate without cause upon six months' written notice. The Company recognized \$5,000,000, \$6,027,000 and \$4,000,000 as revenue under the Schering agreement in 2001, 2000 and 1999, respectively.

Eli Lilly & Company

The Company and Eli Lilly and Company ("Lilly") entered into a collaborative agreement to design inhibitors of the hepatitis C protease enzyme for development as novel drugs to treat hepatitis C infection. Under the terms of the agreement, Lilly agreed to pay the Company up to \$51,000,000 comprised of a \$3,000,000 payment paid in June 1997, \$33,000,000 of product research funding over six years and \$15,000,000 of development and commercialization milestone payments. The Company has the option to supply 100 percent of Lilly's commercial drug substance supply needs. If the Company exercises its commercial supply option, the Company will receive drug supply payments in addition to royalties on future product sales, if any. Lilly has the right to terminate the agreement without cause upon six months' written notice. Revenue recognized under the HCV Protease program under the Lilly contract was \$6,686,000, \$5,948,000, \$5,452,000 in 2001, 2000, 1999, respectively.

Kissei Pharmaceutical Co. Ltd.

P38 MAP Kinase. The Company and Kissei Pharmaceutical Co., Ltd. ("Kissei") entered into an agreement to collaborate on the identification of inhibitors of p38 MAP kinase and the development of those compounds as novel, orally active drugs for the treatment of inflammatory and neurological diseases. Under the terms of the agreement, Kissei agreed to pay the Company up to \$22,000,000 composed of a \$4,000,000 license payment, \$11,000,000 of product research funding over three years and \$7,000,000 of development and commercialization milestone payments. Research funding ended under this program on June 30, 2000 and the Company has received the full amount of research funding specified under the agreement. Kissei has exclusive rights to develop and commercialize certain compounds in Japan and various Southeast Asian countries and semi-exclusive rights in China, Taiwan

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

O. Significant Revenue Arrangements (Continued)

and South Korea. The Company retains exclusive marketing rights in the United States, Canada, Europe and the rest of the world. In addition, the Company will have the right to supply bulk drug material to Kissei for sale in its territory and will receive royalties and drug supply payments on future product sales, if any. Additionally, Kissei agreed to pay certain development costs. Kissei has the right to terminate the agreement without cause upon six months' notice. In 2001, 2000 and 1999, approximately \$6,248,000, \$5,615,000, and \$6,286,000 was recognized as revenue under the p38 MAP kinase research and development program, respectively.

HIV Protease Inhibitors. The Company and Kissei are collaborating in the development and commercialization of amprenavir. Under the collaborative agreement, Kissei agreed to pay the Company up to \$20,000,000, comprised of \$9,800,000 of product research funding through 1995, \$7,000,000 of development milestone and territory option payments and a \$3,200,000 equity investment. The Company received the full amount of research funding specified under the agreement. Under the collaboration, Kissei has exclusive rights to develop and commercialize amprenavir in Japan and will pay Vertex a royalty on sales. Vertex is responsible for the manufacture of bulk product for Kissei. Revenue earned under the Kissei agreement in 2001, 2000 and 1999 were \$1,157,000, \$7,000, and \$1,000,000, respectively.

GlaxoSmithKline

The Company and GlaxoSmithKline ("Glaxo") entered into a collaborative agreement to develop and commercialize Agenerase (amprenavir) and its prodrug VX-175. Under the collaborative agreement for research and development of HIV protease inhibitors, Glaxo agreed to pay the Company up to \$42,000,000 comprised of a \$15,000,000 license payment paid in 1993, \$14,000,000 of product research funding over five years and \$13,000,000 of development and commercialization milestone payments for an initial drug candidate. Glaxo is also obligated to pay additional development and commercialization milestone payments for subsequent drug candidates, including VX-175. Research funding under this agreement ended on December 31, 1998. In addition, Glaxo is required to bear the costs of development in its territory of drug candidates under the collaboration. Glaxo has exclusive rights to develop and commercialize Vertex HIV protease inhibitors in all parts of the world except the Far East and will pay Vertex a royalty on sales. The Company has retained certain bulk drug manufacturing rights and certain co-promotion rights in territories licensed to Glaxo. Glaxo has the right to terminate its arrangement without cause upon twelve months' notice. Termination of the agreement by Glaxo will relieve it of its obligation to make further commercialization and development milestone and royalty payments and will end any license granted to Glaxo by Vertex under the agreement. In 1999, the Company began earning a royalty from Glaxo from sales of Agenerase. Revenues and royalties earned from Glaxo were \$11,211,000, \$15,646,000, and \$13,927,000 in 2001, 2000 and 1999, respectively.

In June 1996, the Company and Glaxo obtained a worldwide, non-exclusive license under certain G.D. Searle & Co. ("Searle") patent applications in the area of HIV protease inhibition. The Company pays Searle a royalty based on sales of Agenerase.

Assay Development, Screening Services and Instrumentation Agreements

Aurora has certain contracts under which it agrees to sell instrumentation systems and technology licenses, in addition to providing assay development and screening services. Each of these separable elements may be individually delivered and are not considered essential to the functionality of one another. The Company allocates revenue under such contracts to each of the separable elements based

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

O. Significant Revenue Arrangements (Continued)

on its relative fair value which under most of our agreements approximates the stated price in the contract.

Pfizer and Warner-Lambert (acquired by Pfizer in 2000)

Prior to the acquisition of Warner-Lambert by Pfizer in 2000 the Company had separate contracts with each company. Following the acquisition, the Company continued to deliver on the individual contracts until the contracts were amended and consolidated in 2001. The revenues recognized from such contracts for 1999, 2000 and 2001 are as follows:

	<u>2001</u>	<u>2000</u>	<u>1999</u>
	(In thousands)		
Pfizer			
Product sales (instrumentation and technology licensing)	\$12,298	\$15,955	\$ 9,542
Assay development and screening services	6,357	2,877	1,184
Warner-Lambert			
Product sales (instrumentation and technology licensing)	4,926	4,739	6,867
Assay development and screening services	55	2,125	2,695
	<u>\$23,636</u>	<u>\$25,696</u>	<u>\$20,288</u>

Following the amendment and consolidation of the contracts the Company has a continuing obligation to deliver instrumentation and technology licenses. If such commitments are delivered and accepted the Company will record as much as \$12,000,000 in revenue.

P. Employee Benefits

The Company has a 401(k) retirement plan (the "Vertex 401(k) Plan") in which substantially all of its permanent employees are eligible to participate. Participants may contribute up to 20% of their annual compensation to the plan, subject to statutory limitations. The Company may declare discretionary matching contributions to the Vertex 401(k) Plan which are payable in the form of Company shares. The match is paid in fully vested Company shares and employees have the ability to transfer funds from Company stock as they choose. The Company declared matching contributions to the Vertex 401(k) plan as follows (in thousands except per share data):

	<u>2001</u>	<u>2000</u>	<u>1999</u>
Discretionary matching contributions for the year ended December 31, . .	\$ 1,399	\$ 1,148	\$ 866
Shares issued for the year ended December 31,	15,215	20,880	47,708
Shares issuable as of the year ended December 31,	32,284	10,000	13,400

In connection with the acquisition of Aurora in July 2001, the Company assumed the Aurora 401(k) Retirement Savings Plan and 401(k) Profit Sharing Plan Trust (collectively, the "Aurora Plan") covering substantially all employees of Aurora and its wholly-owned subsidiaries who have completed certain service requirements. Participants may contribute a portion of their compensation to the Aurora Plan through payroll deductions. Company-paid Aurora Plan matching contributions, if any, are determined by the Company at its sole discretion and payable in the form of cash. The Company's cash contributions under the Aurora Plan totaled \$453,000, \$338,000 and \$225,000 in 2001, 2000 and 1999, respectively.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

Q. Related Party

A sibling of the Company's Chairman and Chief Executive Officer was a partner in a law firm representing the Company to which \$200,000, \$736,000 and \$480,000 in legal fees were paid in 2001, 2000 and 1999, respectively. As of September 24, 2001 he is no longer a partner with that firm and was hired as Senior Vice President and General Counsel of Vertex.

In April 2001, Aurora entered into an agreement with a customer, which included assay development services, product sales and licenses combined with the purchase of stock in the customer. At the time of the transaction, the Chief Executive Officer of the customer was a director of Aurora. As of July 18, 2001, following the acquisition of Aurora by Vertex, the Chief Executive Officer of the customer is no longer a director of Aurora. The total investment in the customer is approximately \$4,120,000 at December 31, 2001 and represents approximately 6% of the outstanding equity interest of the customer. The Company believes that the amounts charged by the Company for services, products and licenses are comparable to what the Company would have charged had it not purchased the stock in the customer and had the former director of Aurora not been affiliated with the customer. The investment is accounted for using the cost method and is included in Investments on the balance sheet. Total revenue recognized from this agreement in 2001 was \$3,348,000.

As of December 31, 2001, the Company had a loan outstanding to a director in the amount of \$132,000. The loan was interest free and was forgiven in January 2002 as a result of a retention and non-compete agreement executed by the Company in April 2001.

In 2001, the Company entered into a consulting agreement with a director of the Company for the provision of part-time consulting services over a period of four years at \$80,000 per year, commencing in January 2002.

R. Legal Proceedings

Chiron Corporation filed suit on July 30, 1998 against Vertex and Eli Lilly and Company in the United States District Court for the Northern District of California, alleging infringement by the defendants of three U.S. patents issued to Chiron. The infringement action relates to research activities by the defendants in the hepatitis C viral protease field and the alleged use of inventions claimed by Chiron in connection with that research. Chiron has requested damages in an unspecified amount, as well as an order permanently enjoining the defendants from unlicensed use of the claimed Chiron inventions. During 1999, Chiron requested and was granted a reexamination by the U.S. Patent and Trademark Office of all three of the patents involved in the suit. Chiron also requested and, over the opposition of Vertex and Eli Lilly, was granted a stay in the infringement lawsuit, pending the outcome of the patent re-examination. That reexamination proceeding is still on-going and the stay is still in effect. However, a Notice of Intent to Issue a Reexamination Certificate has been issued in two of the three Chiron patents in suit. While the length of the stay and the final outcome of the lawsuit cannot be determined, Vertex maintains that Chiron's claims are without merit and intends to defend the lawsuit, if and when it resumes, vigorously.

On December 7, 2001 Oregon Health Sciences University filed suit against Vertex in the District Court of Oregon. The complaint in the suit seeks to name Dr. Bruce Gold, an employee of Oregon Health Sciences University, as an inventor and Oregon Health Sciences University as part owner of five of Vertex's neurophilin patents. The suit stems from assays run on Vertex compounds by Dr. Gold under a sponsored research agreement in 1996. Vertex has investigated the inventorship on these patents and believes that Dr. Gold is not an inventor, Oregon Health Sciences has no ownership interest in any of these patents, and that the claims made in this complaint are without merit. Vertex intends to contest this claim vigorously.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

S. Segment Information

The accounting policies of the segments are described in the summary of significant accounting policies (Note B). The Company evaluates segment performance based on loss before merger related charges, debt conversion costs, the cumulative effects related to changes in accounting principles and extraordinary items. The Company does not evaluate segment performance based on the segment's total assets and therefore the Company's assets are not reported by segment. The following tables contain information about results for the years ended December 31, 2001, 2000 and 1999.

<u>(In thousands)</u>	<u>Vertex</u>	<u>Aurora</u>	<u>Total</u>
Year Ended December 31, 2001:			
Revenues	\$ 77,408	\$91,370	\$168,778
Inter-segment revenue	—	(1,288)	(1,288)
Interest income	39,894	5,239	45,133
Interest expense	(18,671)	(647)	(19,318)
Depreciation and amortization	(13,534)	(4,430)	(17,964)
Equity in losses of unconsolidated subsidiary	(662)	—	(662)
Reportable segment income (loss)	<u>\$(56,875)</u>	<u>\$12,108</u>	<u>\$(44,767)</u>
Year Ended December 31, 2000:			
Revenues	\$ 78,127	\$75,155	\$153,282
Inter-segment revenue	—	—	—
Interest income	27,679	5,633	33,312
Interest expense	(10,569)	(1,084)	(11,653)
Depreciation and amortization	(9,095)	(3,697)	(12,792)
Equity in losses of unconsolidated subsidiary	(550)	—	(550)
Reportable segment income (loss)	<u>\$(22,122)</u>	<u>\$ 4,918</u>	<u>\$(17,204)</u>
Year Ended December 31, 1999:			
Revenues	\$ 50,560	\$58,327	\$108,887
Inter-segment revenue	—	—	—
Interest income	11,088	1,866	12,954
Interest expense	(654)	(1,050)	(1,704)
Depreciation and amortization	(6,206)	(3,465)	(9,671)
Equity in losses of unconsolidated subsidiary	(724)	—	(724)
Reportable segment loss	<u>\$(40,966)</u>	<u>\$ (188)</u>	<u>\$(41,154)</u>
	<u>2001</u>	<u>2000</u>	<u>1999</u>
Total loss for reportable segments	\$(44,767)	\$(17,204)	\$(41,154)
Merger related charges	(23,654)	—	—
Debt conversion costs	—	(14,375)	—
Cumulative effect of changes in accounting principles—revenue recognition	(25,901)	(3,161)	—
Cumulative effect of change in accounting principle—derivatives	17,749	—	—
Extraordinary gain on early extinguishment of debt	10,340	—	—
Total net loss	<u>\$(66,233)</u>	<u>\$(34,740)</u>	<u>\$(41,154)</u>

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

T. Quarterly Financial Data (unaudited)

(in thousands, except per share data)

	Three Months Ended			
	March 31, 2001*	June 30, 2001*	Sept. 30, 2001	Dec. 31, 2001
Revenues:				
Royalties	\$ 2,596	\$ 2,862	\$ 2,592	\$ 3,069
Product sales	11,529	15,423	13,442	19,527
Service revenues	5,258	6,083	6,445	9,680
Collaborative and other research and development revenues	15,573	16,273	17,889	19,249
Total revenues	<u>34,956</u>	<u>40,641</u>	<u>40,368</u>	<u>51,525</u>
Costs and expenses:				
Royalty payments	881	972	880	1,053
Cost of product sales	6,371	6,314	6,815	5,742
Cost of service revenues	2,589	2,169	2,968	2,875
Research and development	31,963	33,969	38,116	44,625
Sales, general and administrative	12,224	12,729	11,991	10,393
Merger related costs	1,179	4,363	15,751	2,361
Total costs and expenses	<u>55,207</u>	<u>60,516</u>	<u>76,521</u>	<u>67,049</u>
Loss from operations	(20,251)	(19,875)	(36,153)	(15,524)
Interest income	13,070	11,768	12,223	8,072
Interest expense	(5,003)	(4,879)	(4,927)	(4,509)
Debt conversion expense	—	—	—	—
Other, net	(30)	(392)	(372)	(1,639)
Loss before cumulative effect of changes in accounting principles and extraordinary items	<u>(12,214)</u>	<u>(13,378)</u>	<u>(29,229)</u>	<u>(13,600)</u>
Cumulative effect of changes in accounting principle—revenue recognition (Note C)	(25,901)	—	—	—
Cumulative effect of changes in accounting principle—derivatives (Note H)	—	—	17,749	—
Extraordinary gain on early extinguishment of debt (Note K)	—	—	—	10,340
Net loss	<u>\$(38,115)</u>	<u>\$(13,378)</u>	<u>\$(11,480)</u>	<u>\$ (3,260)</u>
Basic and diluted net loss per common share	\$ (0.52)	\$ (0.18)	\$ (0.15)	\$ (0.04)
Basic and diluted weighted average number of common shares outstanding	73,922	74,381	74,682	74,926

* Prior 2001 quarterly financial results have been restated for the retroactive adoption of the Substantive Milestone Method of revenue recognition to January 1, 2001. Please refer to "Note C: Change in Accounting Principle—Revenue Recognition" in the notes to the consolidated financial statements for further information.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

T. Quarterly Financial Data (unaudited) (Continued)

	Three Months Ended			
	March 31, 2000	June 30, 2000	Sept. 30, 2000	Dec. 31, 2000
Revenues:				
Royalties	\$ 2,686	\$ 3,393	\$ 3,309	\$ 2,973
Product sales	10,060	15,917	13,809	12,651
Service revenues	4,843	4,330	5,068	6,004
Collaborative and other research and development revenues	5,830	24,087	14,664	23,658
Total revenues	<u>23,419</u>	<u>47,727</u>	<u>36,850</u>	<u>45,286</u>
Costs and expenses:				
Royalty payments	907	1,145	1,194	888
Cost of product sales	6,795	8,495	8,059	7,778
Cost of service revenues	2,166	2,140	2,043	2,008
Research and development	21,560	23,679	26,230	29,624
Sales, general and administrative	10,613	11,245	11,028	13,128
Total costs and expenses	<u>42,041</u>	<u>46,704</u>	<u>48,554</u>	<u>53,426</u>
Loss from operations	(18,622)	1,023	(11,704)	(8,140)
Interest income	4,432	9,063	9,243	10,574
Interest expense	(1,168)	(2,762)	(2,666)	(5,057)
Debt conversion expense	—	—	(14,375)	—
Other, net	(38)	(297)	(722)	(363)
Income (loss) before cumulative effect of change in accounting principle	<u>(15,396)</u>	<u>7,027</u>	<u>(20,224)</u>	<u>(2,986)</u>
Cumulative effect of changes in accounting principle— revenue recognition (Note C)	(3,161)	—	—	—
Net income (loss)	<u><u>\$(18,557)</u></u>	<u><u>\$ 7,027</u></u>	<u><u>\$(20,224)</u></u>	<u><u>\$ (2,986)</u></u>
Basic net income (loss) per common share	\$ (0.29)	\$ 0.11	\$ (0.30)	\$ (0.04)
Diluted net income (loss) per common share	\$ (0.29)	\$ 0.10	\$ (0.30)	\$ (0.04)
Basic weighted average number of common shares outstanding	64,526	66,064	67,462	72,662
Diluted weighted average number of common shares outstanding	64,526	73,940	67,462	72,662



Corporate Information

Executive Officers

Joshua S. Boger, Ph.D.

Chairman and Chief Executive Officer

Vicki L. Sato, Ph.D.

President

Michael G. Wokasch

President, Aurora Biosciences and PanVera Corporation

John J. Alam, M.D.

Senior Vice President, Drug Evaluation and Approval

Kenneth S. Boger

Senior Vice President and General Counsel

N. Anthony Coles, M.D., MPH

*Senior Vice President, Commercial Operations —
Pharmaceutical Products*

Lynne H. Brum

*Vice President, Corporate Development
and Communications*

Iain P.M. Buchanan

*Vice President of European Operations and Managing
Director of Vertex Pharmaceuticals (Europe) Limited*

Ian F. Smith

Vice President and Chief Financial Officer

Board of Directors

Joshua S. Boger, Ph.D.

*Chairman of the Board, Chairman and Chief Executive
Officer, Vertex Pharmaceuticals Incorporated*

Barry M. Bloom, Ph.D. * *

*Formerly Executive Vice President for
Research and Development, Pfizer Inc.*

Roger W. Brimblecombe, Ph.D., D.Sc. *

*Formerly Executive Vice President for Research and
Development (Europe and Japan), SmithKline French
Laboratories*

Stuart J. Collinson, Ph.D.

*Partner, Forward Ventures and formerly Chairman of the
Board, Chief Executive Officer and President, Aurora
Biosciences Corporation*

Donald R. Conklin * *

*Formerly Executive Vice President,
Schering-Plough Corp.*

Bruce Sachs °

*General Partner, Charles River Ventures and formerly
CEO of Stratus and formerly CEO of Xylogics*

Charles A. Sanders, M.D. °

Formerly Chairman and Chief Executive Officer, Glaxo Inc.

Elaine Ullian *

President and Chief Executive Officer, Boston Medical Center

Scientific Advisory Board

Mark Murcko, Ph.D.

*Chair of the Scientific Advisory Board
Vice President and Chief Technology Officer
Vertex Pharmaceuticals Incorporated*

Vicki L. Sato, Ph.D.

President

Vertex Pharmaceuticals Incorporated

Steven J. Burakoff, M.D.

*Laura and Isaac Perlmutter Professor, New York University
School of Medicine; Director, New York University Cancer
Institute; Director, Skirball Institute of Biomolecular Medicine*

Eugene H. Cordes, Ph.D.

*Professor of Medicinal Chemistry
College of Pharmacy
Adjunct Professor of Chemistry
College of Literature, Science, and the Arts
University of Michigan, Ann Arbor*

Stephen C. Harrison, Ph.D.

*Higgins Professor of Biochemistry, Harvard University;
Investigator, Howard Hughes Medical Institute; Professor
of Biological Chemistry and Molecular Pharmacology and
Professor of Pediatrics, Harvard Medical School*

Jeremy R. Knowles, D.Phil.

*Amory Houghton Professor of Chemistry
and Biochemistry, Harvard University*

Robert T. Schooley, M.D.

*Tim Gill Professor of Medicine and Head of the Division of
Infectious Diseases, University of Colorado Health Sciences Center*

Dr. Roger Tsien, Ph.D.

*Investigator, Howard Hughes Medical Institute; Professor of
Pharmacology and Professor of Chemistry and Biochemistry,
University of California, San Diego*

Safe Harbor Statement

This annual report contains forward-looking statements about Vertex and some of its potential drug development candidates, including statements relating to the expansion of Vertex's product pipeline in the coming year, the selection of additional new drug development candidates, the ability of Vertex to bring drug candidates through clinical development, the expectation of additional corporate collaborations, and the potential for the acquisition of new and complementary technologies. While management makes its best efforts to be accurate in making forward-looking statements, any such statements are subject to risks and uncertainties that could cause actual results to vary materially. These risks include the possibility of delays in the selection of potential drug candidates and preclinical studies. These risks also include the possibility of delays in clinical trials as a result of delays in planned patient enrollment among other things, the risk that clinical trials may not result in a marketable product, the possibility that complementary technologies will not be available to the Company on acceptable terms, if at all, and the risk that Vertex may be unable to successfully finance, secure regulatory approval of and market any of its current or future drug candidates.

Shareholder Information

Corporate Headquarters

Vertex Pharmaceuticals Incorporated

130 Waverly Street
Cambridge, MA 02139-4242
617.444.6100
617.444.6680 (fax)

Annual Meeting

The annual meeting of shareholders will be held on May 17, 2002 at 9:30 a.m. at Vertex Pharmaceuticals Incorporated, 130 Waverly Street, Cambridge, MA.

Auditors

PricewaterhouseCoopers LLP
One Post Office Square
Boston, MA 02109

Legal Counsel

Kirkpatrick & Lockhart LLP
75 State Street
Boston, MA 02109

Mintz Levin Cohn Ferris Glovsky and Popeo PC

One Financial Center
Boston, MA 02111

Patent Counsel

Fish & Neave
1251 Avenue of the Americas
New York, NY 10020

Investor Inquiries

617.444.6100
617.444.6680 (fax)
investorinfo@vrtx.com

Transfer Agent & Registrar

EquiServe, Limited Partnership
Shareholder Services Department
P.O. Box 8040
Boston, MA 02266-8040
(781) 575-3120
www.equiserve.com

Correspondence concerning transfer requirements and lost certificates should be directed to the above address.

Visit Vertex's web site at: <http://www.vrtx.com>

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* Member of the Compensation Committee

° Member of the Audit Committee

+ Member of the Nominating Committee



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